

THE BRITISH JOURNAL OF DERMATOLOGY NOVEMBER 1952

OBSERVATIONS ON THE RELATIONSHIP OF THE SWEAT DUCTS TO POMPHOLYX VESICLES.

DENIS CHARLES DEVINE, M.D.

From the Department of Dermatology, Glasgow Western Infirmary
Group Hospitals.

TILBURY FOX (1873) described a sago-grain vesicular eruption of the hands which he called dysidrosis. He attributed the condition to a retention of sweat in the ducts at rete level. Since his time, however, many have come to regard the lesions as a manifestation of an eczematous reaction (Williams, 1891; Sicoli, 1924 (pseudodysidrosis); Peck, 1930 (most cases); McLachlan and Brown, 1934; MacLeod and Muende, 1940; Sequeira *et al.*, 1947; Percival *et al.*, 1947). Even so there have always been those who support the original concept of Fox or concede its possibility in certain cases (Duhring, 1881; Nestorowsky, 1906; Sicoli, 1924 (dysidrosis); Peck, 1930; McCarthy, 1931). There are others also whose opinions appear to be *sub judice*, but who are inclined to favour some sweat-duct association (e.g., Sulzberger and Baer, 1948). Again some authorities, not necessarily ascribing the lesions to a disordered sweat mechanism, have at times indicated the proximity of duct and vesicle (Robinson, 1885; Radcliffe-Crocker, 1893; Unna, 1896; Sutton, 1913).

In the course of the study of more than a thousand serial sections of nine specimens of pompholyx vesicles arising either as part of a generalized sensitization dermatitis, in association with atopic eczema or apparently idiopathically in the presence of palmar hyperidrosis, certain constant observations were made. With regard to these, it was considered essential by a comparison of specimens and by reference to the literature to establish an identity of lesions of different aetiological origin because findings from the various specimens selected were correlated to establish conclusions referring to a common process. Clinically similar vesicles, therefore, of apparently different aetiological origins were examined at the outset with this purpose in mind.

THE CORRELATION OF CLINICAL SIMILARITY OF VESICLES WITH SIMILAR HISTOLOGY.

McLachlan and Brown (1934) indicated the histopathological similarity of lesions having scabietic, idiopathic and occupational origins and others associated with eczema of other parts. Comparison of their photographs with one of Peck's (1930) which was thought to be of fungous origin seems to show no point of variance. This apparent identity was corroborated in the present series.

A lesion arising in the absence of apparent cause in a case of palmar hyperhidrosis presents an apparently identical lesion with that from a patient in whom the pompholyx eruption was part of a generalized sensitization dermatitis. The appearances in both cases are of rounded and often multilocular fluid-filled spaces containing the rudiments of degenerated prickle cells, confined to the rete, the corium usually showing minimal non-specific change. A specimen from the idiopathic group (Fig. 1) shows no essential difference.

All other specimens studied supported this histological similarity, corroborating the observations of McLachlan and Brown that the lesions are a common reaction to different causes.

RELATION OF POMPHOLYX VESICLES TO THE SWEAT DUCTS OF THE EPIDERMIS.

In view of the substantial school of opinion which has either upheld or conceded the possibility that pompholyx eruptions are the result of a sweat retention in the epidermis the following findings are published.

Fig. 2 shows one of a series of sections through a small vesicle in relation to a sweat duct. Throughout its intra-epidermal course it is close to the vesicle, but fails at all levels to communicate with it. Normal cohesion of cells around the duct appears to exist and no fluid spaces can be seen between them. The figure shows the only duct in the vicinity of the vesicle, which together with its surrounding prickle cells is apparently normal though those immediately adjacent show signs of degeneration. The portion of the duct shown in Fig. 1 is actually passing between the walls of two vesicles, the pale cells indicated (x) being a vesicular wall cut tangentially. The duct is cut transversely at the arrowhead. A darkened line of relatively compact cells follows its main course, suggesting that they are probably the least affected of the prickle cells involved in the degenerative changes. The gland glomerulus appears normal and cellular infiltration is absent.

Serial sections show that some vesicles are unrelated to any duct whatsoever.

Figs. 1 and 2 represent sections from cases of different causes. Thus Fig. 1 is from an idiopathic case associated with palmar hyperhidrosis, and Fig. 2 from a patient who had a generalized sensitization dermatitis of the papulo-

vesicular type of which the pompholyx eruption appeared to be a manifestation. The vesicles in both cases were entirely independent of sweat ducts. The rete in relation to a sweat duct in Fig. 1 appears to show less degeneration than the surrounding cells as inferred from its more deeply staining character.

At this point it has so far been demonstrated that no connection appears to exist between pompholyx vesicles and the intra-epidermal portion of the sweat ducts even in idiopathic cases associated with palmar hyperhidrosis. The structural lining of the only ducts in relation to many vesicles was seen to be

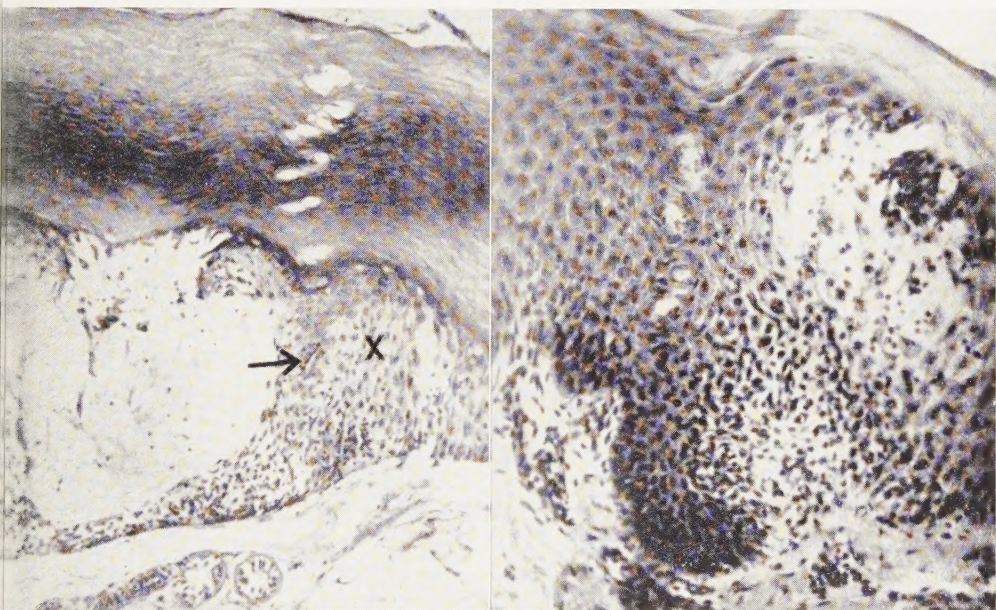


FIG. 1.—Lesion from an idiopathic case with palmar hyperhidrosis. Arrowhead indicates where duct is cut transversely. X denotes a vesicular wall cut tangentially. H. & E. $\times 130$.

FIG. 2.—An apparently normal duct passes between two vesicles. The relatively pale cells to the left of the duct represent a vesicular wall cut tangentially. Serial section examination showed the duct to be entirely extra-vesicular. H. & E. $\times 210$.

intact, and no abnormal fluid spaces were noted between the cells to suggest sweat extravasation. No duct distention was ever observed.

SWEAT DUCT RESISTANCE TO CHANGES FOUND IN PRICKLE CELLS.

The fact that sweat ducts found in the vicinity of early vesicles seemed to escape the processes involving the adjacent rete suggested that they offered some degree of resistance. A vesicle was never seen in the early stages to disturb the cohesion of a duct. When it formed in the neighbourhood of one of these structures the latter usually lay undisturbed adjacent to the vesicular

wall, or as occasionally happened the duct was seen to traverse the vesicular cavity (Fig. 3).

Fig. 2 shows a sweat duct passing between the walls of two vesicles. The cavity of the one on the right is clearly shown. To the left of the duct the pale cells of a vesicular wall cut tangentially can be seen. The sweat duct and its adjacent prickle cells appear relatively normal although adjacent cells show various degrees of degeneration.

A similar though less marked example is demonstrated in Fig. 1 in which the relatively dense area representing a duct and surrounding prickle cells is shown to pass undisturbed between the walls of two vesicles, the cavity of the one on the right again being not apparent as the section passes tangentially to its wall, the cells of which appear to be in a state of degeneration.

As already indicated, Fig. 3 depicts a duct passing through the vesicular cavity. Serial sections showed that the portions on either side of the duct were actually part of the one cavity. In Fig. 4 serial sections indicate that the ducts in the vesicular walls are at all times extra-vesicular. In Fig. 5 three ducts are in relation to the vesicle, two within the wall and another in the partition dividing the loculi. The middle and right duct pass along the thin floor separating the lesion from the corium.

Fig. 6 shows vesicles which were intravitally injected with 0.5% aqueous trypan blue. Nothing existed to indicate that the dye gained access to the duct shown, other than by simple diffusion. The duct can be observed passing through the vesicular cavity, the surrounding prickle cells having been involved in the pathological reaction whilst the duct would seem to remain unaffected.

Fig. 7 exemplifies a high-power field of a vesicle cut in transverse section. The arrowhead indicates a duct, its bulging suggesting a relative rigidity of structure.

From a study of the foregoing illustrations it is apparent that the sweat ducts in their intra-epidermal course withstand for a considerable time the processes affecting the adjacent prickle cells in pompholyx vesiculation. It is thus inferred that they are not the seat of pompholyx vesiculation. It is further emphasized that not only are the ducts not primarily involved in the reaction, but they are singularly spared in the initial stages.

THE RELATIONSHIP OF TISSUE DIFFERENCES TO DISINTEGRATIVE CHANGES.

It has been observed that the degenerative process whatever be its cause fails, originally at least, to disturb the cohesion of the sweat ducts. This apparently singular resistance of the latter structures was the subject of further investigation to determine if their component cells differed in any way from the adjacent prickle cells. The literature on this subject indicates that no established view is held regarding the identity of cells constituting duct struc-



FIG. 3.

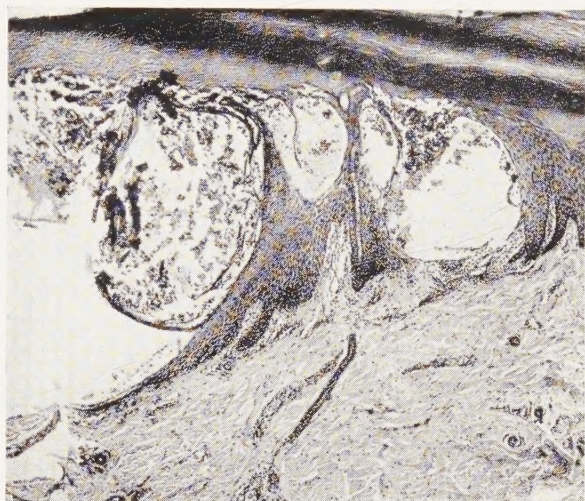


FIG. 4.



FIG. 5.



FIG. 6.

FIG. 3.—A sweat duct is seen passing vertically through a vesicular cavity. The prickly cells surrounding the duct have undergone dissolution but the duct cells have maintained their cohesion. H. & E. $\times 120$.

FIG. 4.—A duct is seen passing between vesicles. Serial section examination demonstrated that in no part of its course did it communicate with a vesicle. H. & E. $\times 50$.

FIG. 5.—Three ducts are shown. The left is passing into the partition dividing the loculi. The middle and right ducts are passing under the floor and a little way up the vesicular wall. (The dark material within the vesicle is intra-vitally injected indian ink which had no relation to the present investigation.) H. & E. $\times 55$.

FIG. 6.—The stratum granulosum (G) and sweat ducts (S) are seen to have a similar affinity for trypan blue. Carmalum. $\times 55$.

ture within the rete. Some authorities maintain that it is a channel without walls among the prickle cells (Way and Memmesheimer, 1936; Maximow and Bloom, 1948). MacLeod and Muende (1940) do, however, indicate that the stratum granulosum dips down to form a funnel for the duct, which at a deeper level is merely a spiral cleft among the prickle cells. Pinkus (1939) on the other hand emphasized that ducts possess a structural lining, which he concluded was apparent by the manner in which the component cells often escape morbid changes affecting the surrounding prickle cells. He further indicated that in acute vesicular eczema the prickle cells around a duct may disappear, leaving that structure intact. With the above conflicting hypotheses in view some ducts were carefully examined by serial section.

Fig. 8 shows a normal sweat duct. As it passes through the stratum granulosum in a downward direction it appears to acquire this layer as a wall which, as indicated by granules, seems to reach the level of rete pegs. It was noted, however, in most specimens examined that the number of granules per cell diminished with the depth in the rete and often in the lowest layers they had entirely disappeared. The prickle cells immediately adjacent to the duct are spindle-shaped, while those further removed are polyhedral. This was a fairly constant finding. In a few cases a downward transition from basophilic to eosinophilic staining of granules was noted in the cells of duct walls.

Fig. 6 shows a multilocular vesicle intra-vitally injected with trypan blue. A certain affinity for the dye is apparent in certain cells. The deeply staining areas of the vesicular roof represent the stratum granulosum. The upper portion of the inter-vesicular partition is also deeply stained. The maximum intensity is, therefore, shown to correspond to the upper transitional layers and rapidly diminishes with the depth, the polyhedral cells being unstained. The intra-epidermal portion of the sweat duct demonstrated in the same specimen shows a similar staining; like the stratum granulosum proper it also has affinity for this stain.

This similar staining property when correlated with similar histological features indicates that the cells of the rete portion of the sweat duct, if not identical with those of the stratum granulosum proper, are closely related in character to them. From a study of these specimens, therefore, it appears that in the greater part of their intra-epidermal course the walls of the sweat ducts are composed of stratum granulosum-like cells. Further close examination indicates an absence of tonofibrils. This is in keeping with the appearance of those granulosum cells proper which lie immediately adjacent to the stratum lucidum. The surrounding prickle cells are spindle-shaped and more compact than normal (Fig. 8). Their appearances and relationship to the lining granular cells of the ducts suggest morphological similarity to the few layers of prickle cells which in the epidermis normally underlie the stratum granulosum.

The closely similar nature of the intra-rete portion of the ducts and stratum

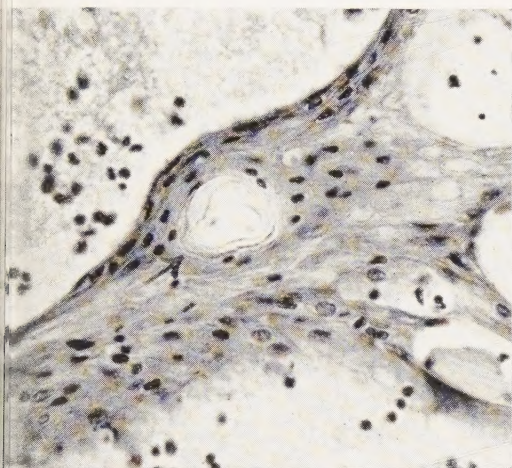


FIG. 7.

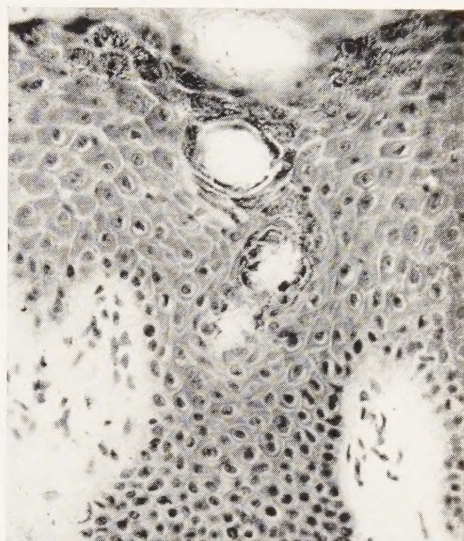


FIG. 8.

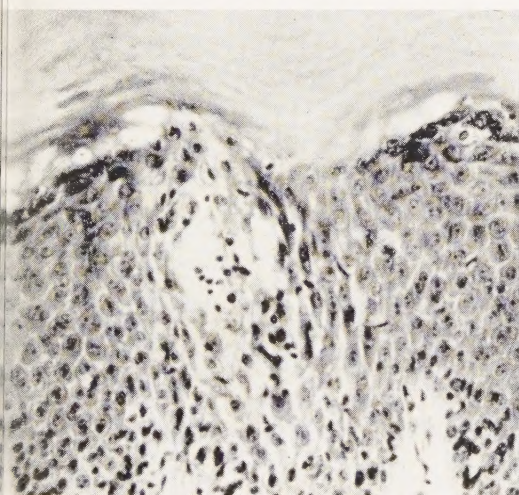


FIG. 9.

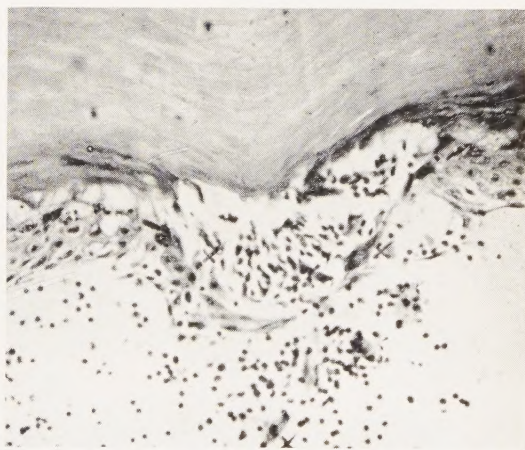


FIG. 10.

FIG. 7.—The arrowhead indicates a duct cut transversely. H. & E. $\times 420$.

FIG. 8.—Granular cells in the wall of all normal sweat ducts are seen at the level of the rete pegs. H. & E. $\times 420$.

FIG. 9.—Early vesicle showing in the roof pale staining stratum granulosum cells which have lost their granular appearance. H. & E. $\times 275$.

FIG. 10.—The summit of a vesicle roof. x denotes relatively intact stratum granulosum cells. H. & E. $\times 360$.

granulosum was further substantiated by observations made regarding their common resistance to disintegration. It has already been observed that the cells of the ducts initially withstand the disintegrative changes affecting the prickle cells in pompholyx vesiculation. In the earliest vesicles examined (Fig. 9) the stratum granulosum was always affected as part of the original focus of degeneration. This was determined by eosinophilic changes in the cells and by loss of granules. Although local cleavage between the cells of this layer followed (Fig. 10), almost invariably this loss of cohesion was not observed to occur as the result of the cytoplasmic dissolution which affected the underlying prickle cells. The cytoplasm of affected granulosum cells remained intact long after that of the prickle cells had completely disappeared (Fig. 10). It appears, therefore, that the cells of the intra-rete portion of the sweat ducts have a relative immunity, in common with the granulosum cells proper, to the dissolution which affects the prickle cells in pompholyx vesiculation.

It is, therefore, inferred that the component cells of the intra-rete portion of the sweat ducts are closely related in type to those of the stratum granulosum proper.

CONCLUSIONS.

Observations confirm the histopathological similarity of pompholyx vesicles of different aetiology.

The sweat ducts in the rete withstand for a considerable time the processes affecting the adjacent prickle cells in pompholyx vesiculation.

Apart from the ducts not being primarily involved in the reaction they are singularly spared in the initial stages. This depends upon the duct cells differing from prickle cells, and being more akin to the cells of the stratum granulosum.

The microphotographs published in this paper are selected from a series submitted to the University of Glasgow as part of an M.D. thesis (December 1949).

I wish to thank Dr. James Sommerville for his most valuable advice and criticism. I wish also to acknowledge much of the inspiration for this article to the paper of Dr. A. D. MacLachlan and Dr. W. H. Brown.

REFERENCES.

- DUHRING, L. A. (1881) *A Practical Treatise on Diseases of the Skin*. 2nd ed. Philadelphia: J. B. Lippincott & Co., p. 229.
- FOX, T. (1873) *Skin Diseases*. 3rd ed. London: H. Renshaw, p. 476.
- MAXIMOW, A. A., and BLOOM, W. (1948) *A Textbook of Histology*. 5th ed. Philadelphia and London: W. B. Saunders Company, p. 345.
- MCCARTHY, L. (1931) *Histopathology of Skin Diseases*. London: H. Kimpton, p. 472.
- MACLACHLAN, A. D., and BROWN, W. H. (1934) *Brit. J. Derm. Syph.*, **46**, 457.
- MACLEOD, J. M. H., and MUENDE, I. (1940) *Practical Handbook of the Pathology of the Skin*. 2nd ed. London: H. K. Lewis & Co. Ltd., p. 252.
- NESTOROWSKY, W. A. (1906) *Derm. Z.*, **13**, 183 (quoted by Pringle, J. J., and Adamson, H. G. (1911) *System of Medicine*, edited by Allbutt, T. C., and Rolleston, H. D. 2nd ed. London: Macmillan and Co., **9**, 665).
- PECK, S. M. (1930) *Arch. Derm. Syph., Chicago*, **22**, 40.

- PERCIVAL, G. H., DRENNAN, A. M., and DODDS, T. C. (1947) *Atlas of Histopathology of the Skin*. Edinburgh : E. & S. Livingstone, Ltd., p. 135.
- PINKUS, H. (1939) *J. invest. Derm.*, **2**, 175.
- RADCLIFFE-CROCKER, H. (1893) *Diseases of the Skin*. 2nd ed. London : H. K. Lewis & Co. Ltd., p. 166.
- ROBINSON, A. R. (1885) *A Manual of Dermatology*. New York : D. Appleton & Co., p. 246.
- SEQUEIRA, J. H., INGRAM, J. T., and BRAIN, R. T. (1947) *Diseases of the Skin*. 5th ed. London : J. & A. Churchill, Ltd., p. 162.
- SICOLI, A. (1924) *Ann. Derm. Syph., Paris*, 6e sér., **5**, 69.
- SULZBERGER, M. B., and BAER, R. L. (1948) *The 1948 Year Book of Dermatology and Syphilology*. Chicago : The Year Book Publishers, p. 25.
- SUTTON, R. L. (1913) *J. Amer. med. Ass.*, **61**, 240.
- UNNA, P. G. (1896) *The Histopathology of the Diseases of the Skin*, translated by Walker, N. Edinburgh : William F. Clay, p. 177.
- WAY, S. C., and MEMMESHEIMER, A. (1936) *Arch. Derm. Syph., Chicago*, **34**, 797.
- WILLIAMS, A. W. (1891) *Brit. J. Derm. Syph.*, **3**, 303.
-

SWEAT DUCTS AND THE POMPHOLYX VESICLE.

HAROLD WILSON, M.D., M.R.C.P.,

Dermatologist, Central Middlesex Hospital ; First Assistant, Skin Department,
Middlesex Hospital, W.1.

AND

A. C. THACKRAY, M.A., M.D.,

Reader in Morbid Anatomy and Histology, Middlesex Hospital Medical School, W.1.

UNDER the title "dysidrosis" Tilbury Fox (1873) described the occurrence of a vesicular eruption on the palms and soles. He regarded the condition as separate from eczema, and believed it to result from sweat retention. Hutchinson (1876) used the name cheiropompholyx to describe an identical disorder. He found that it was commoner in hot weather and tended to afflict nervous subjects ; he did not, however, consider that Fox had proved his theory of sweat retention.

Other workers (Thin, 1877 ; Robinson, 1877) examined the contents of the vesicles and found that its chemical composition differed from that of sweat. In later publications Fox (Fox, 1877 ; Fox and Radcliffe-Crocker, 1878) reiterated his theory, believing that those who did not endorse his views were misled either by an incomplete histological examination or by their confusion of a secondary inflammatory lesion with the primary retention one. Fox's observations were unconfirmed by the work of Williams (1891) and of Sutton (1913), neither of whom was able to trace any definite relationship between the vesicles and the coil glands or their ducts. Pusey (1911), however, believed this condition to be exactly analogous to miliaria in other parts, the clinical differences resulting only from the presence of a thickened horny layer on the palms and soles. A similar opinion was expressed recently by Whimster (1950). He examined seven vesicles removed post-mortem from the hands of a boy of six who had suffered from cheiropompholyx every summer for three or four years before his death. In each case continuity could be demonstrated between the vesicles and the lumen of the sweat duct. Examination of a vesicle from a second subject showed its histological character to be eczematous, and Whimster was forced to the conclusion that there are two pathologically distinct types of pompholyx vesicles, the one dysidrotic and the other eczematous.

In an attempt to elucidate this problem we record here our findings in seven cases of typical cheiropompholyx in each of which biopsies were performed.

CASE REPORTS.

CASE 1.—R. P—, male, aged 41 ; B.O.A.C. captain.

History.—For 10 to 15 years had suffered from recurrent attacks of small blisters on hands and occasionally feet. Eruption begins within a day or two of arrival in a hot climate, and clears a week after return to this country. Treated with x rays in 1944 and 1947 with clearance of the rash for 2 and 4 years respectively. Present attack began a month ago and has persisted.

Examination.—Symmetrical vesicular eruption on both hands. No hyperidrosis. Feet clear.

Histology.—Over 300 serial sections of this lesion were studied. It consisted of a single vesicle situated in the prickle-cell layer with the thick stratum corneum over it, and containing albuminous fluid and occasional cells—lymphocytes, polymorphs and large mononuclears in approximately equal numbers. There were collections of similar inflammatory cells mainly around small blood vessels in the superficial part of the dermis. There were sweat glands on either side of the vesicle, but none in its immediate vicinity, and no ducts opening into it.

CASE 2.—J. G. M—, male, aged 52 ; overseer in G.P.O.

History.—Began as a blister on the left hand two years ago. A year later symmetrical blisters appeared on both hands, and these have continued to come up at frequent intervals ever since.

Examination.—Vesicular eruption on palms and backs of both hands ; no hyperidrosis. Feet clear.

Histology.—Microscopic examination showed a single unilocular vesicle in the prickle-cell layer, the overlying stratum corneum being of normal thickness. Moderate numbers of inflammatory cells in the vesicle, mainly polymorphs and lymphocytes with groups of similar cells in the superficial part of the dermis. Sweat ducts were followed in serial sections on either side of the vesicle but none approached close to it.

CASE 3.—J. C—, male, aged 37 ; hairdresser's manager.

History.—In the past 2 years has had 10–12 attacks of blisters on one or both hands, mainly the palms and sides of the fingers, and occasionally on the feet. Attacks last 2–3 weeks, and are worse in the summer and during periods of mental anxiety.

Examination.—Symmetrical vesicular rash on palms of hands and sides of fingers. Hyperidrotic. Feet clear.

Histology.—Thick stratum corneum over the lesion, which consisted of a dozen or so small vesicles lying in the superficial part of the Malpighian layer and separated from each other by strands of stretched-out prickle cells. Some of these septa showed degeneration of the component epithelial cells ; others had broken across, leaving frayed ends. Inflammatory cells present were mainly lymphocytes and large mononuclears. Two sweat ducts followed in serial sections had been pushed aside by the lesion.

CASE 4.—D. B—, female, aged 17 ; machinist.

History.—Eight years of symmetrical vesicular rash affecting the palms and backs of both hands. Attacks last 1–3 months and occur every 3–6 months, winter and summer. Two months before attending hospital both feet became affected. Mental upset appeared to precipitate attacks.

Examination.—Discrete vesicles on hands and feet. Hyperidrotic. No fungus found.

Histology.—Serial sections showed a thin horny layer overlying a complex lesion made up of a large number of locules of various sizes. The locules were separated in places by intervals of normal epidermis, but in other places only by thin columns or sheets of stretched-out epithelial cells. In the septa separating adjoining locules



FIG. 1. Section from Case 4 showing a sweat duct, cut obliquely in three places, running in the septum separating two of the several locules which make up the lesion. $\times 200$.

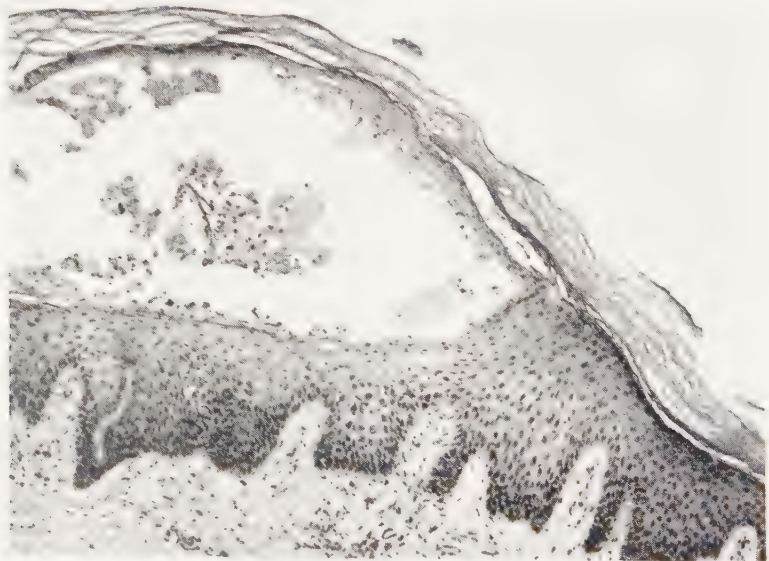


FIG. 2. The lesion from Case 5. Its roof is thin and its floor is keratinized. To the left () a sweat duct in the epidermis is seen just before opening into the cavity of the vesicle. $\times 80$.

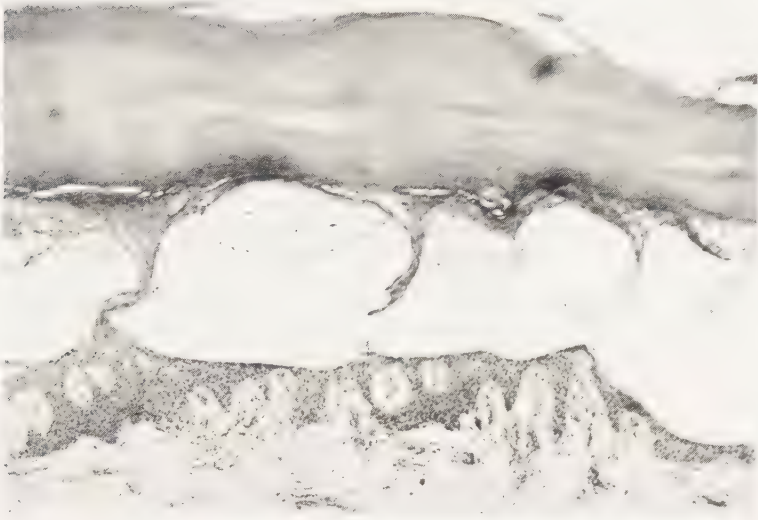


FIG. 3.—The central part of the lesion from Case 6. The septum on the left is intact, that at the centre has just ruptured, while that on the right shows necrosis of its cells and fraying of its free end. $\times 70$.

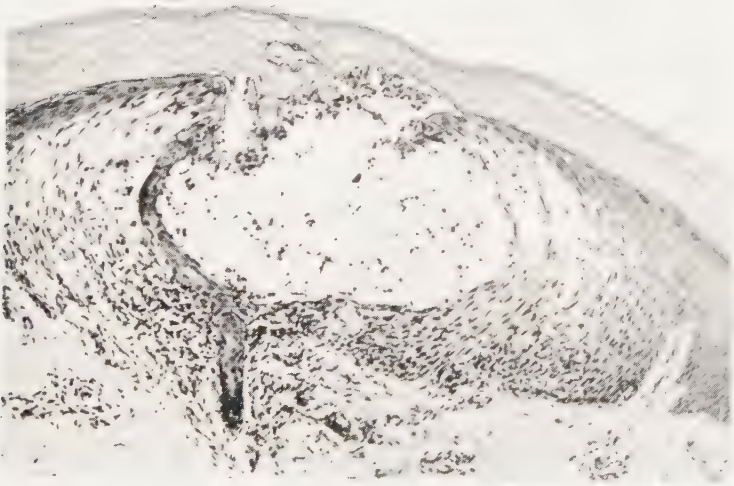


FIG. 4.—A sweat duct displaced to the left of a typical eczematous vesicle in Case 7. $\times 95$.
VOL. 64.

surviving sweat ducts could sometimes be found (Fig. 1). Numbers of inflammatory cells in the vesicle fluid, mainly lymphocytes and large mononuclears.

CASE 5.—A. L—, male, aged 43 ; clerk.

History.—Eight years ago a rash began in E. Africa on the palms and backs of both hands, and persisted until he left Africa two years later. Cleared a few months after returning to England, but has recurred intermittently since then. Attacks now last 2 weeks and recur every 3–4 months, being worse in summer. Feet are now affected more than hands.

Examination.—Discrete transparent vesicles on hands and feet. Hyperidrotic. No fungus found.

Histology.—Sections showed a large old vesicle, with a few small younger lesions around it. The main lesion was regarded as old because its walls had consolidated and the epithelial cells forming its floor had keratinized (Fig. 2), whilst the horny layer forming its roof had almost all been shed. Two otherwise normal sweat glands opened into the floor of the vesicle ; this was the only lesion studied into which sweat ducts actually opened. The vesicle contained inflammatory cells, many of them swollen and necrotic, similar to those seen in the other cases.

CASE 6.—C. B—, female, aged 18.

History.—Two years' eruption of blisters on hands, palms and backs. Recurrent attacks during the summer, with freedom throughout the winter. Temporary improvement following x rays. Suffers from asthma.

Examination.—Symmetrical vesicular eruption on both hands. Hyperidrotic. Feet clear.

Histology.—Sections showed several vesicles of various sizes lying in the prickle-cell layer ; the overlying stratum corneum was thick. The stretched-out strands of epithelial cells separating the vesicles were undergoing necrosis and breaking down, a process which would eventually have resulted in the production of one large vesicle (Fig. 3). Sweat glands deep to the lesion and ducts in its immediate neighbourhood appeared normal.

CASE 7.—A. W—, male, aged 33 ; manager.

History.—For one month has had blisters on both hands, particularly the palms and fingers. Small group of blisters on left foot. A similar condition 10 years ago which cleared up after 4 months.

Examination.—Symmetrical vesicular eruption on the palms and sides of the fingers of both hands. Feet clear. No fungus found.

Histology.—A young vesicle with fluid amongst the prickle cells bounding it. The lesion was unilocular and confined to the prickle-cell layer. A sweat duct followed in serial section was deflected by the lesion (Fig. 4) ; no ducts were seen opening into it.

DISCUSSION.

Pompholyx frequently affects hyperidrotic subjects, and attacks are undoubtedly commoner during periods of hot weather. It is probable that some association lies between the eruption and excessive sweating, and it would be convenient to explain the lesion as a simple dilatation of a sweat duct. The examination of vesicles from these seven cases, however, gives no support to the theory that the primary disorder in this condition is an accumulation of retained sweat. The sequence of events appears to us to be as follows : The lesion originates amongst the prickle cells as an accumulation of fluid which

breaks through the intercellular bridges to form a typical eczematous vesicle. Sweat ducts in the neighbourhood of the growing vesicle are either displaced laterally (Fig. 4), or survive as trabeculae or septa running through it (Fig. 1). These trabeculae at a later stage may undergo necrosis (Fig. 3), so that in an occasional mature vesicle sweat ducts may be seen opening through the floor.

It is commonly believed (Way and Memmesheimer, 1936; MacLeod and Muende, 1946; Percival, Murray Drennan and Dodds, 1947) that the sweat in the epidermis merely travels through a tract in the cells and that the duct here has no cohesion, although Pinkus (1939) held a contrary opinion and published photomicrographs showing sweat ducts within the epidermis. Our findings, particularly in Case 5, suggest that the cells lining the sweat channel are more firmly united than those of the prickle-cell layer in general, so that the sweat channel may persist as a hollow column of cells in the midst of the vesicle.

SUMMARY.

Serial sections of typical lesions from seven cases of pompholyx provide no evidence that the vesicle results from sweat retention.

REFERENCES.

- FOX, T. (1873a) *Brit. med. J.*, **2**, 365.
— (1873b) *Amer. J. Syph. Derm.*, **4**, 1.
— (1877) *Brit. med. J.*, **2**, 798.
— and RADCLIFFE-CROCKER, H. (1878) *Trans. path. Soc. Lond.*, **29**, 264.
HUTCHINSON, J. (1876) *Lancet*, **1**, 630.
MACLEOD, J. M. H., and MUENDE, I. (1946) *Practical Handbook of the Pathology of the Skin*, 3rd ed. London: H. K. Lewis & Co. Ltd., p. 252.
PERCIVAL, G. H., DRENNAN, A. M., and DODDS, T. C. (1947) *Atlas of Histopathology of the Skin*. Edinburgh: E. & S. Livingstone, Ltd., p. 7.
PINKUS, H. (1939) *J. invest. Derm.*, **2**, 175.
PUSEY, W. A. (1911) *The Principles and Practice of Dermatology*, 2nd ed. New York and London: D. Appleton & Co., p. 948.
ROBINSON, A. R. (1877) *Arch. Derm.*, **3**, 289.
SUTTON, R. L. (1913) *J. Amer. med. Ass.*, **61**, 240.
WAY, S. C., and MEMMESHEIMER, A. (1936) *Arch. Derm. Syph., Chicago*, **34**, 797.
WHIMSTER, I. (1950) *Brit. J. Derm.*, **62**, 32.

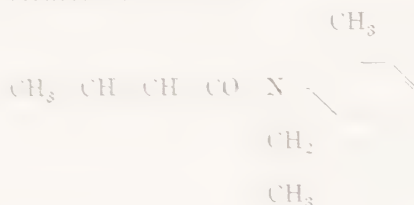
AN EVALUATION OF N-ETHYL-O-CROTONOTOLUIDE AS AN ANTIPRURITIC.

M. HITCH, M.D.,

Raleigh, North Carolina, U.S.A.

Two specific antipruritic properties of N-ethyl-o-crotonotoluide now seem reasonably well established on the basis of several publications in both European and American literature.

This substance, which was originally reported on by Domenjoz in 1946, was assigned the following structural formula :



It is evident that it is not chemically related to the "caines" or to the group of compounds currently regarded as antihistaminics. In like manner its chemical configuration appears entirely foreign to such simple antipruritics as phenol and camphor or to the complex tars. Hence considerable interest has been aroused in this new addition to dermatological medicaments.

The original investigations of Domenjoz concerned the value of many chemical compounds as parasitocides, and he ultimately demonstrated that N-ethyl-o-crotonotoluide in various reasonable concentrations was a better substance for this purpose (against *Psoroptes cuniculi*). It was simultaneously shown to have bacteriostatic action on streptococci, staphylococci and *C. diphtheriae*. Domenjoz further demonstrated it to be relatively non-toxic in animal ingestion experiments and to cause little irritation on animal skin.

The first reported clinical use of N-ethyl-o-crotonotoluide was by Burckhardt and Rymarowicz (1946) who were evaluating it in the treatment of scabies. Their results seemed to show that it not only was excellent for this purpose, but also possessed considerable antibacterial action and did not irritate eczematized scabious lesions. They were the first to comment on its immediate antipruritic effect.

The following year Lenggenhager (1947), attesting the excellent antiscabietic properties of 10% N-ethyl-o-crotonotoluide in a washable ointment base, reported a rather large number of local and systemic reactions—all of which were presumably transitory. No subsequent investigator has recorded such an alarming proportion of side-effects.

Subsequent observations of the acaricidal properties of this compound have

been made by von Roten (1947), Dorner (1949), Couperus (1949), Tronstein (1949), Patterson (1950), Appel (1950), Hand (1950), and Peck and Michelfelder (1950). In addition, several of these investigators found it effective against pediculi.

Whether the chemical has been used as a parasiticide or as a general topical antipruritic most investigators have commented on the relative freedom from side reactions, systemic toxicity, local irritation, and sensitivity reactions. For example, Couperus (1949) followed the general application of a 10% ointment in 20 subjects with blood counts and urine examinations and failed to demonstrate any type of toxicity which might be reflected in these examinations. No reports to date, except that of Lenggenhager, have recorded detectable symptoms of systemic toxicity.

The low sensitizing index of the chemical has been indicated by both Couperus and Peck and Michelfelder (1950). The former patch-tested 170 individuals, 30 of whom were re-tested, and found no reactions of sensitivity or primary irritation from the drug itself. In 30 of 70 subjects the pure chemical was tested, while in the remainder a 10% concentration in a washable ointment base or petrolatum was used. Four persons showed weakly positive reactions, but in each of these the washable ointment base was demonstrated to be the offending substance. In clinical use, 70 patients with scabies and 124 with various dermatoses were treated by Couperus, with sensitization or irritation in only three cases. In these the reactions were mild and were likewise shown to be due to the vehicle.

Peck and Michelfelder, employing a two-week usage test on individuals with normal skin, failed to demonstrate primary irritation or sensitivity to N-ethyl-o-crotonotoluide. Two of their subjects showed transitory erythema which was proved to be due to the base. However, one patient in Peck and Michelfelder's group of 80 with various dermatoses developed a sensitivity to the chemical itself. Soifer (1950) noted four examples of intolerance to the 10% concentration in washable ointment base among 97 cases, but felt that these represented irritation of an existing dermatitis rather than sensitivity since these same individuals tolerated the preparation on other areas.

Tronstein (1949) treated 199 cases of scabies without evidence of systemic toxicity, sensitization, or appreciable local irritation. He also reported but little irritation when the preparation was brought in contact with the conjunctiva. Similar observations have been made by others, including Hand (1950). Patterson (1950) treated 120 cases of scabies without observing side reactions, and Appel (1950) intimates that a similar situation prevailed in his treatment of 87 patients with scabies. Soifer (1951) found eight patients intolerant to the cream. Four of these were sensitive to the vehicle, and the remainder were not tested. Pierce (1951) cured 73 of 84 patients with scabies without reaction or side-effects.

It appears then that sufficient data have accumulated to demonstrate that N-ethyl-o-crotonotoluide is a fair bactericide, an excellent parasiticide (properties which will not be treated here), non-toxic and without side reactions in effective concentrations, relatively non-irritant to normal skin, and with quite a low sensitizing index. The last attribute is extremely important if its use as a general antipruritic in common chronic dermatoses is contemplated. Peck and Michelfelder have emphasized this in comparison with the benzocaine group and the antihistaminics.

The virtue of N-ethyl-o-crotonotoluide as a topical antipruritic was first remarked by Burekhardt and Rymarowicz (1946), and subsequently by most of the investigators mentioned above. Although the immediate relief of itching in scabies comprises most of the material on this subject, Couperus, Peck and Michelfelder, and Soifer have systematically studied the antipruritic properties of the preparation in many non-parasitic dermatoses. In 124 patients with various pruritic complaints Couperus obtained excellent relief in 66.2%, moderate relief in 27.4%, and poor results in but 6.4%. Peck and Michelfelder, reporting on 80 patients with similar complaints, apparently obtained "good" or "complete" relief in 28 and "fair" or better in most of the remainder, while Soifer said that the antipruritic effect of this compound was excellent in 83.7% of 117 patients suffering from a variety of itching dermatoses. Johnson and Bringe (1951) encountered "complete" or "considerable" relief in 74.3%

RESULTS OF TREATMENT.

The material dealt with here consists of a strictly clinical evaluation of the first 200 patients on whom an adequate follow-up could be obtained. Practically all were from private practice. The medicament used throughout was a 10% dilution of N-ethyl-o-crotonotoluide in a vanishing cream base.* No selection of patients was made except on the basis of (i) the presence of pruritus, and (ii) the assumption that the use of this preparation would not have a deleterious effect. Previous reports and early personal experiences indicated that skin in an acute, exudative or vesicular stage tolerates the cream poorly, and this class of case was in large measure excluded from the study. In most patients with dermatitis venenata the acute stage had passed before the cream was applied. Race, age, sex and complexion did not seem to be influencing factors and are excluded from the tabulations.

The duration of this topical medication varied from a few days to several weeks. Patients with mild eruptions were often relieved in several days and were free of a recurrence. These are included, since it did not seem that in

* States by Geigy Pharmaceuticals as Eurax cream. In Great Britain it is issued in 5% concentration in combination with an anti-histamine, name of Teevex.

TABLE I.—*Relief of Pruritus.*

	Number of patients.	Excellent.	Good.	Slight.	None.	Influence on eruption.
<i>Neurodermatoses.</i>						
Atopic dermatitis	9	2	5	2	0	3
Circumscribed neurodermatitis	15	5	4	2	4	6
Disseminated neurodermatitis	51	20	16	12	3	20
Neurotic excoriations	2	0	1	0	1	1
Pruritus ani, vulvae, scroti	23	12	5	5	1	3
	100	39	31	21	9	33
		70%		30%		
<i>Eczematoid dermatoses.</i>						
Chronic contact dermatitis	13	4	5	3	1	2
Infantile eczema	5	1	1	1	2	2
Nummular eczema	2	0	0	2	0	0
Stasis dermatitis	5	4	1	0	0	5
	25	9	7	6	3	7
		64%		36%		
<i>Toxic and allergic erythemas.</i>						
Dermatitis medicamentosa	2	1	1	0	0	1
Erythema multiforme	1	0	0	0	1	0
Unclassified	7	5	1	1	0	1
	10	6	2	1	1	2
		80%		20%		
<i>Dermatoses due to living organisms.</i>						
Creeping eruption	2	0	0	0	2	0
Dermatophytosis (feet)	1	0	0	1	0	0
Herpes simplex	1	0	1	0	0	0
Herpes zoster	2	1	0	1	0	0
Infectious eczematoid dermatitis	1	1	0	0	0	1
Moniliasis (vulvae)	3	0	1	1	1	0
Sycosis vulgaris	1	0	0	1	0	0
Tinea corporis	1	0	1	0	0	0
Varicella	1	0	0	1	0	0
	13	2	3	5	3	1
		38%		62%		
<i>Miscellaneous dermatoses.</i>						
Acanthosis nigricans	1	0	0	1	0	0
Aerodynia (subsiding)	1	0	1	0	0	0
Bath pruritus	1	0	0	0	1	0
Dermatitis herpetiformis	1	0	1	0	0	0
Dermatitis venenata	12	2	4	4	2	0
Exfoliative dermatitis	1	0	1	0	0	0
Lichen planus	2	0	1	0	1	0
Lichen urticatus	4	0	2	2	0	1
Lupus erythematosus (subacute)	1	0	0	0	1	0
Miliaria rubra	3	1	1	0	1	1
Pityriasis rosea	13	3	5	3	2	0
Psoriasis	2	2	0	0	0	0
Schamberg's disease	3	1	1	1	0	0
Scleroderma (vulvae)	1	0	0	0	1	0
Seborrhoeic dermatitis	3	2	0	0	1	1
Senile pruritus	3	1	2	0	0	0
	52	12	19	11	10	3
		60%		40%		
Totals	200	68	62	44	26	46
		65%		35%		

such a strictly clinical evaluation a minimum treatment time was significant if relief had been complete and relapse had not occurred in a reasonable period.

The form of investigation and results presented here are essentially similar to those of Couperus and of Peck and Michelfelder. Because of the difficulties inherent in evaluating a patient's degree of relief from pruritus this approximate agreement in results is perhaps significant.

In the classification of results used here and summarized in Table I "excellent" means complete relief from itching for at least eight hours or throughout the night; "good" implies complete relief for a slightly shorter period, the patient finding it desirable to use the preparation three or four times daily; "slight" relief signifies something less than complete absence of pruritus even with an application of the remedy every two or three hours. The segregation of "good" from "excellent" results was particularly rigid, and either category can be considered indicative of a satisfactory antipruritic effect. For this reason these two groups are taken together in the percentages in Table I. With these standards it will be seen that 34% obtained very gratifying results, 31% were considerably benefited, 22% received some relief, and but 13% were unaffected.

When questioned about the degree of relief obtained with N-ethyl-o-crotonotoluide cream patients were asked to compare it with other topical remedies which had been used. These ranged from rubbing alcohol to complex antipruritic lotions and ointments. The most commonly encountered antipruritic substances were probably phenol, antihistaminics, and the benzocaine and tar groups. In 115 cases such information was available. Although it is fully appreciated that this subjective evaluation is treacherous, perhaps *in toto* it has some significance: 76.6% of those reporting a comparative appreciation of the medicament under consideration favoured it over all previously employed (Table II).

Except in parasitic eruptions and perhaps in those dermatoses whose aetiology is entirely or partly dependent on local bacterial activity, there seems to be no pharmacological reason to expect visible improvement from the use of this preparation. Nevertheless, as shown in Table I, appreciable objective improvement did ensue in a number of patients.

No evaluation of benefit from the emollient and protective properties of the vehicle was made and no clear-cut examples of the Koebner phenomenon were seen.

Local reactions were minimal. A transient sensation of warmth, especially about the genitalia, was occasionally reported but was not objectionable. Six patients objected to the medicament on the grounds that it was more or less irritating. These cases and the results of patch-testing are tabulated in Table III. One patient with a mild dermatitis venenata about the ankles could not be followed. Two patients suffering from chronic pruritus vulvae et ani spoke

TABLE II.

	Number of patients reporting.	More relief than all other local applications.	Less relief than some local applications.
<i>Neurodermatoses.</i>			
Atopic dermatitis	6	5	1
Circumscribed neurodermatitis	9	6	3
Disseminated neurodermatitis	35	30	5
Neurotic excoriations	2	1	1
Pruritus ani, vulvae, scroti	18	14	4
	70	56	14
<i>Eczematoid dermatoses.</i>			
Chronic contact dermatitis	5	4	1
Infantile eczema	3	2	1
Nummular eczema	1	0	1
Stasis dermatitis	3	3	0
	12	9	3
<i>Toxic and allergic erythemas.</i>			
Dermatitis medicamentosa	1	1	0
Unclassified	4	3	1
	5	4	1
<i>Dermatoses due to living organisms.</i>			
Herpes simplex	1	1	0
Herpes zoster	1	0	1
Infectious eczematoid dermatitis	1	1	0
Moniliasis (vulvae).	2	1	1
Tinea corporis	1	1	0
	6	4	2
<i>Miscellaneous dermatoses.</i>			
Dermatitis herpetiformis	1	1	0
Dermatitis venenata	6	4	2
Exfoliative dermatitis	1	1	0
Lichen planus	2	0	2
Lupus erythematosus (subacute)	1	0	1
Miliaria rubra	2	2	0
Pityriasis rosea	2	1	1
Psoriasis	1	1	0
Schamberg's disease	1	1	0
Seborrhoeic dermatitis	3	2	1
Senile pruritus	2	2	0
	22	15	7
Totals	115	88	27
		76·6%	23·4%

TABLE III.—Results of Patch Test.

Diagnosis.	Patient No.	10% N-ethyl- o-crotono- toluide cream.	N-ethyl- o-crotono- toluide.	Cream base.	10% N-ethyl- o-crotono- toluide in petrolatum.
Neurodermatitis disseminata	1	+	+++	0	—
Pruritus vulvae et ani	2	0	0	0	—
Dermatitis venenata	3	—	—	—	—
Circumscribed neurodermatitis	4	0	0	0	0
Pruritus vulvae et ani	5	0	0	0	0
Monilial vulvovaginitis	6	—	—	—	—

vaguely of objectionable qualities of the medicament, but had no objective evidence of irritation or hypersensitivity. The patient with circumscribed neurodermatitis reported that the application was antipruritic for an "hour or so" but then caused burning and erythema. This was not observed in the consulting room, and patch-testing failed to explain the complaint. Patient 6 with an acute monilial vulvovaginitis associated with pregnancy employed other topical remedies simultaneously and may have suffered irritation from a combination of chemicals: or the dermatitis may have been too acute to tolerate the medicament. It has been impossible to carry out patch tests on this patient, so that hypersensitivity to the active ingredient or vehicle cannot be ruled out. Patient 1 suffered from a rather severe generalized neurodermatitis. Approximately one month before the adverse reaction she had used the cream off and on for a period of seven weeks not only without difficulty but with moderate symptomatic benefit. Her reaction after a general application of the medicament consisted of violent burning and a moderate erythema visible ten hours later, though the skin was cleansed shortly after onset of the reaction. As seen in Table III, this patient was hypersensitive to N-ethyl-o-crotonotoluide.

COMMENT.

It appears from previously published reports and the material presented here that in N-ethyl-o-crotonotoluide there has been added to the dermatological armamentarium a topical antipruritic of considerable merit. Its mode of action remains undetermined, but the experimental studies by Kwoczek in Germany seem to indicate that the pharmacological activity of this substance, exclusive of its parasitocidal action, is restricted entirely to suppression of the sensation of itching. Employing an appreciable number of human subjects, he produced localized pruritus with histamine and scarification and then compared the effects of topical antihistaminics with those of N-ethyl-o-crotonotoluide. The latter proved superior. These findings partly contradict those of Melton and Shelley (1950), who were unable to demonstrate an antipruritic effect on experimental histamine pruritus with any of an extensive array of substances including two antihistaminics. In further studies Kwoczek compared the effects of N-ethyl-o-crotonotoluide and antihistaminic ointments on other dermal sensations. In testing the effects of these compounds on the appreciation of heat, cold, touch, pain, and tickling, he found no alteration with N-ethyl-o-crotonotoluide, whereas in most instances the antihistaminics exerted a mild anaesthetic action, reducing the acuteness of all the sensations tested except that of pain. This lack of anaesthetic activity of N-ethyl-o-crotonotoluide, if corroborated by further studies, may recommend it in many pruritic conditions.

All patients included here complained of considerable itching, even those with dermatoses such as Schamberg's disease or psoriasis, which do not usually itch

The over-all satisfactory response of 65% is comparable with the results obtained by Couperus and by Peck and Michelfelder. Perhaps it is correct to say that those patients classified as obtaining "slight" relief benefited to about the same degree as with the usual antipruritic lotions and ointments exclusive of the antihistaminics in selected cases. Table I indicates that the best symptomatic relief may be expected in the neurodermatoses and "toxic" erythemas, though the latter group is perhaps too small to be indicative. Poor results are evident in the group of eruptions due to living organisms. In the miscellaneous dermatoses there are scarcely sufficient cases of a single disease except pityriasis rosea and dermatitis venenata to have individual significance. However, when considered *in toto* this heterogeneous group responded rather well (60% satisfactory relief). Why two patients with psoriasis were relieved of itching while two with lichen planus received much less benefit is not clear. Nevertheless, in patients suffering from one of the disorders in this miscellaneous group, the use of N-ethyl-o-crotonotoluide as a symptomatic remedy concurrently with specific treatment is probably worthy of trial.

Since some of these patients had long-standing or relapsing complaints and had employed many other topical medications, their own comparative evaluation of the new remedy was enlightening. Table II shows that such comparison was available for 115 patients. 76.6% of these preferred N-ethyl-o-crotonotoluide to all other local treatment. As would be expected, this preference was more striking in those groups (e.g., the neurodermatoses) exhibiting higher proportions of "excellent" and "good" relief.

The most difficult factor to analyse with confidence was the influence of N-ethyl-o-crotonotoluide cream on the eruption. An attempt was made to allow for spontaneous fluctuations in the appearance of the eruption and to take into consideration the likely effects of other procedures which were employed concurrently with the cream. In self-limiting dermatoses such as pityriasis rosea it was assumed that the topical remedy had no influence on the objective progress. Originally an attempt was made to assess the *degree* of improvement in the eruption. However, this proved impractical, and was abandoned in favour of simply recording presence or absence of improvement. The evaluation of such improvement was entirely clinical, and was recorded only after a sincere attempt had been made to discount the influences of psychotherapy, time, and previous or concurrent treatment. One gained the impression that objective improvement was most apt to occur where there was a large neurogenic element and the eruption was reasonably mild. It seems logical to assume that two factors may operate in the resolution of neurodermatitis with antipruritic therapy alone: traumatism is abolished or greatly reduced, and the absence of itching promotes a feeling of confidence and optimism and allows restful sleep.

The sensitization index of any topical medicament is extremely important.

Previously published data on this factor in regard to N-ethyl-o-crotonotoluide seem to indicate that it is quite low. The 200 cases reported here corroborate this finding inasmuch as it was deemed desirable to perform patch tests on only six patients. In two of these testing was not done. In the remaining four only one was shown to be hypersensitive to N-ethyl-o-crotonotoluide. In contrast to other reports, no example of sensitivity or irritation to the washable ointment base was encountered. In the three remaining patients who complained of moderate discomfort with application of the cream, no explanation was found by patch-testing.

Since there is but slight chemical kinship between N-ethyl-o-crotonotoluide and other substances commonly employed topically or internally, cross sensitization should be encountered rarely. The washable ointment base employed in the commercial preparation has been responsible for most of the reported examples of intolerance. Perhaps it would be desirable to have the pure chemical available for incorporation in various prescriptions or commercially prepared in a variety of vehicles.

SUMMARY.

The literature on the dermatological uses of N-ethyl-o-crotonotoluide is reviewed.

200 patients with various pruritic dermatoses (exclusive of parasitic diseases) treated with a commercial preparation of N-ethyl-o-crotonotoluide in a washable ointment base are presented.

The preparation was found to be an excellent antipruritic, essentially non-irritating except in acute eruptions, without systemic toxicity, and of low sensitizing index. Its mode of action is undetermined.

N-ethyl-o-crotonotoluide is probably especially efficacious as a symptomatic remedy in the neurodermatoses, chronic eczematoid dermatoses and toxic and allergic erythemas.

REFERENCES.

- APPEL, B. (1950) *New Engl. J. Med.*, **243**, 74.
 BURCKHARDT, W., and RYMAROWICZ, R. (1946) *Schweiz. med. Wschr.*, **76**, 1213.
 COLUPPI, S. M. (1949) *J. Invest. Derm.*, **13**, 35.
 DOMENJOZ, R. (1946) *Schweiz. med. Wschr.*, **76**, 1210.
 DORNER, G. (1949) *Dtsch. med. Wschr.*, **3**, 422.
 HAND, E. A. (1950) *J. Mich. med. Soc.*, **49**, 1286.
 JOHNSON, S. A. M., and BRIDGE, J. W. (1951) *Arch. Derm. Syph., Chicago*, **63**, 768.
 KWOCZEK, J. Personal communication from Dr. Albert Hemming, New York.
 LINGGENSEHAGER, R. (1947) *Praxis*, **36**, 465.
 MORTON, F. M., and SHELLEY, W. B. (1950) *J. Invest. Derm.*, **15**, 325.
 PATTERSON, R. L. (1950) *St. med. J., B'ham., Ala.*, **43**, 449.
 PECK, S. M., and MICHELFELDER, T. J. (1950) *N. Y. St. J. Med.*, **50**, 1934.
 PIERCE, JR., H. E. (1951) *J. nat. med. Ass.*, **43**, 107.
 TEN, L. V. (1947) *Ueber chin-venes Antiscabiosum*. Basel: Reinhardt Press.
 SOUPE, A. A. In discussion of Peck and Michelfelder (1950).
 1951) *Quart. Rev. Intern. Med. Derm.*, **8**, 1.
 TRONSTEIN, A. J. (1949) *Ohio St. med. J.*, **45**, 889.

LUPUS ERYTHEMATOSUS TREATED WITH MEPACRINE.

JAMES SOMMERVILLE, M.B., F.R.F.P.S.(G.),

DENIS CHARLES DEVINE, M.D.,

AND

JAMES CAMERON PURSE LOGAN, M.D.

From the Dermatological Unit, Glasgow Western Infirmary Group Hospitals,
and the Department of Dermatology, Glasgow University.

HITHERTO treatment of lupus erythematosus, generally speaking, has been rather unsatisfactory. The apparently striking results claimed with regard to mepacrine (Page, 1951) encouraged and led to the treatment of the following cases, the results of which are now recorded. No method of selection was adopted.

TABLE I.—*Cases of Lupus Erythematosus on Mepacrine Therapy.*

Case No.	Sex.	Age (years).	Type and site of lesion.	Duration of disease		Period of administration of mepacrine (weeks).	Result.
				Years.	Months.		
1	F	42	Chronic discoid. Forehead, face and ears	4	—	20	Excellent.
2	F	42	Chronic discoid, multiple, small. Face	2	8	21	Good.
3	F	29	Chronic discoid. Face, scalp and hands	8	5	20	Excellent.
4	F	40	Chronic discoid, gyrate. Face	8	—	17	Good.
5	F	17	Chronic discoid, multiple. Face	1	11	9	Excellent.
6	F	44	Chronic congestive, multiple. Face and neck	1	8	4	Good. (Defaulted.)
7	F	37	Chronic discoid. Bridge of nose	8	—	19	"
8	F	43	Subacute disseminated. Active on face and fingers	9	—	19	Excellent.
9	F	54	Chronic discoid. Naso-labial folds	20	—	16	Good.
10	F	34	Chronic congestive. Nose and cheeks	10	—	15	Good. (Defaulted.)
11	M	55	Chronic discoid. Single lesion on left cheek	9	—	11	"
12	F	28	Chronic discoid. Point of nose	4	8	11	"
13	M	54	Chronic discoid. Right cheek and neck	1	2	6	" (Defaulted.)
14	M	55	Chronic discoid. Scalp	5	—	4	Slight. (Treatment discontinued because of nausea.)
15	M	50	Chronic congestive, extensive over face	9	6	9	Good.
16	F	16	Chronic congestive. Cheeks	1	5	4	Slight. (Intermittent administration.)
17	M	53	Chronic congestive, extensive. Scalp, face and neck	5	—	20	Excellent.
18	F	20	Chronic discoid, multiple, small. Face	—	11	20	Good +.
19	F	64	Chronic discoid	2	10	5	Nil. (Treatment discontinued because of failure to improve.)
20	M	26	Chronic discoid. Single lesion on right cheek	8	—	12	Good.
21	F	55	Chronic discoid. Single lesion on nose	8	—	15	"
22	F	43	Chronic discoid. Cheeks and tip of left ear	3	—	14	"
23	M	55	Chronic discoid. Scalp and nose	22	—	13	"

Table I indicates that 23 patients of varying age groups, duration and stage of disease were treated with mepacrine with results comparable to those recorded by Page, 19 good to excellent, 3 slight, and one nil. No case of acute

disseminated lupus erythematosus was available for treatment during the six months covered by this survey; one case, however, which could be classified as subacute was included. Page's criteria have been followed regarding the category into which each response has been placed, but in this series the intermediate gradings "slight +" and "good +" have been introduced. "Excellent" results, then, signify either complete disappearance of slight lesions or great improvement in extensive lesions; "good" results signify considerable improvement without complete disappearance of lesions and "slight" stands for "definite but minor improvement."

The dosage used was 0.1 g. mepacrine thrice daily until pigmentation became marked. This rarely occurred before two or three weeks had elapsed. The dose was then reduced to that which maintained pigmentation. In some cases 0.1 g. twice daily was required, but usually 0.1 g. daily was adequate. Temporary increases were sometimes necessary if the maintenance dose failed to sustain the pigmentation.

RESPONSE TO PREVIOUS THERAPY COMPARED WITH MEPACRINE.

Table II records the comparative results of treatment by older methods and mepacrine therapy. The drugs previously exhibited, bismuth, gold,

TABLE II.—*Response to Previous Therapy Compared with Mepacrine.*

Drug.	Number of cases treated.	Average total dose (grammes).	Average total period of administration (weeks).	Number of results classified as—					
				Nil.	Slight.	Slight. +	Good.	Good. +	Excellent.
Bismuth (Bisoxyl)	16	1.7	17	3	6	3	3	—	1
Gold (Myocrisin)	9	1.127	20	5	1	3	—	—	—
Vitamin E (Erbynal)	6	31.1	27	2	2	1	1	—	—
Sodium salicylate (entrosalyl)	8	38.3	19	4	2	2	—	—	—
Nicotinamide	5	7.22	21	1	3	1	—	—	—
Mepacrine	23	15.32	13	1	3	—	11	3	5

vitamin E, sodium salicylate and nicotinamide, gave results which in these cases could be classified mainly as "nil" to "slight": only 4 were classified as "good" and one, receiving bismuth, as "excellent." In contrast the effects of mepacrine were mainly good to excellent. It should be noted, however, that the period of observation of the action of mepacrine was much shorter than the period of administration of some of the other drugs. Whether relapses will occur and whether further treatment with mepacrine will be efficacious remains to be determined in the light of further experience.

ILLUSTRATIVE CASE.

A female aged 42, a housewife, had suffered from lupus erythematosus for 4 years. She originally came to the out-patient department on 15.v.51.

Previous history.—She had attended another hospital since shortly after the beginning of the complaint and had carbon dioxide snow therapy, 10% tannic acid cream, Phenergan and Anthisan tablets and quinine sulphate 2 grains thrice daily and in addition had 3 courses of bismuth (10 injections each 0.1 g.) without benefit.

On examination.—She revealed lupus erythematosus of the chronic, discoid

congestive, small, patchy type, widespread over the forehead and face and extending to the ears.

Treatment.—To begin with she had calamine cream locally, and a course of 10 injections of myocrisin. At the end of the course it was noted that follicular hyperkeratosis was still present, but that erythema had largely subsided. Further myocrisin therapy was contra-indicated owing to the incidence of albuminuria. Treatment with Ephynal 50 mg. thrice daily rising to four times daily was commenced on 31.viii.51. On 28.ix.51 it was recorded that the patient showed no improvement on Ephynal but had become pregnant. (She was last confined 10 years ago.)

On 7 December 1951 treatment with mepacrine 0.1 g. thrice daily was commenced. The lesions at this stage were "very congestive, discoid and confluent on forehead and cheeks." Two weeks later there was already some improvement. Lesions were less congested and the dose was reduced to 0.1 g. twice daily. During the month of January 1952 the lesions became "quieter and paler." The dosage of mepacrine was further reduced to 0.1 g. daily and, after two weeks, suspended for one week on account of very deep pigmentation of the skin. After resumption for 1 week at 0.1 g. twice daily on 25.i.52, dosage was reduced to 0.1 g. daily and has been continued thus, apart from a period of three weeks when the patient was being confined. Recently, on 16.v.52, some signs of renewed activity with erythema at the borders of former lesions on the cheeks necessitated raising the dose to 0.1 g. twice daily. Before this slight exacerbation yellow pigmentation had become minimal and the lesions consisted mainly of residual dark brown-coloured macules.

RESPONSE TO MEPACRINE.

The earliest changes noted were subjective and most frequently occurred during the first week of therapy. Patients said that the skin felt "more normal," was "more pliable" or "had more life in it." Itching or burning usually disappeared after a few days. Flattening and early pallor of congestive lesions was frequently observed during the second week of treatment. Disappearance of scaling was sometimes an early feature.

It was noted that the more susceptible a patient was to pigmentation the more rapid was the response. Generally speaking congestive lesions and widespread inactive scarred lesions seemed to improve more rapidly than small, solitary, chronic plaques. Clearing was dramatic in many cases, but in one case in which face lesions cleared rapidly leaving no trace concomitant finger lesions responded much more slowly.

In one case treatment was stopped on account of nausea. No other side-effects were noted. Treatment was suspended in a few cases on account of deep yellow pigmentation.

The results achieved in the present series of cases confirm Page's important observations, and suggest that mepacrine is the drug of choice in the treatment of lupus erythematosus. Whilst there is no certainty that lesions will not relapse, it is hoped that further therapy will be efficacious should this occur. In some cases a maintenance dose of 0.1 g. daily may be required for an indefinite period. The very low incidence during the war of side-effects resulting from the prolonged use of the drug in malaria prophylaxis suggests that maintenance therapy should not involve any great risk.

REFERENCE.

ROYAL SOCIETY OF MEDICINE.

SECTION OF DERMATOLOGY.

President—Dr. G. B. DOWLING.

21 February 1952.

An Epidemic Follicular Eruption.—Dr. R. E. BOWERS.

This is a preliminary account of an epidemic follicular eruption which appeared in Cheltenham early in January 1952.

Clinical picture. The majority of patients are children and young adults, but no age is exempt; the extremes so far are ten weeks and seventy years. Both sexes are affected; there is an apparent excess incidence in young females.

They rarely suffer any constitutional upset, and the rash appears suddenly, sometimes with itching, which is never severe. Some children vomit once at the onset; a few have a slight fever—not above 100° F.—and a generalized lymphadenopathy. The spleen has not been felt in any patient.

The early stage is a papular erythematous follicular eruption. Mostly the face and back are affected, particularly the forehead and mastoid areas; the arms are quite frequently involved, the abdomen occasionally, and the legs seldom (Figs. 1 and 2).

Some of the lesions show comedo formation in the early stages; three or four days later all patients show a variable degree of horny plugging in the follicle mouths; the plugs protrude, particularly on the back, and give a true nutmeg-grater feel to the skin.

After four to ten days the skin returns to its original state, leaving no sequelae.

So far three patients have had second attacks.

White-cell counts in 6 cases showed an eosinophilia of 2–6%; differential counts otherwise normal. Four had a mild leucopenia, but the total white-cell counts were done on oxalated blood and may not be reliable. Five counts were repeated on fresh blood after a week; the totals were normal, but the mild eosinophilia persisted.

Pathology.—Sections taken from 2 patients on the second and third days of the rash, respectively show collagen oedema, maximal around the follicles in 1 patient, but generalized in the other.

Dr. Ian Whimster commented that the appearance was that of an urticaria, and suggested that it might be due to an antigen entering the skin through the follicles. He thought that the horny plugging in the later stages of the eruption was secondary to the perifollicular oedema.

In the earliest stages the horny layer shows no sign of damage.

Comment.—Dr. G. B. Dowling drew my attention to the paper by Schuppli (1947) reporting an outbreak of follicular keratosis in Basle in 1946.

Comparison of Schuppli's description and photographs with the patients affected in the present outbreak makes it seem probable that we are dealing with the same entity; the only differences are as follow:

(1) Schuppli's cases seem often to have lasted more than two months; with one or two exceptions, ours have cleared in ten days at the most.

(2) Schuppli reported some peculiar variants in the later stages of the epidemic; these have not yet been seen here. He discussed the possible relationship of his epidemic to those reported by Brooke in 1893, Rocamora in 1922 and Gougerot *et al.* in Paris in 1944, and it would seem that the later epidemics may well correspond on with the other.

Schuppli was unable to find a cause for his epidemic, which lasted through much of 1946, and died away in the autumn.

On 30 March 1952 Dr. Morley, Medical Officer of Health, Cheltenham, informed me that a certain water reservoir was brought into action after three months' disuse on 5 January. The subsequent course of events was as follows:

Reservoir on 5 January. First cases 7 January. Off 13 January. Last cases 14 January. On 1 February. More cases 3 February. Off 15 February. Last cases 17 February.

It was turned on again from 3 to 23 March, and 6 cases—some of them relapses—were reported from the girls' school on 7, 8 and 10 March, but I am aware of only one outside the school, who was affected on 7 March.

It therefore seems reasonable to suspect the reservoir of brewing some allergen, and that the latter has now become diluted, or the population immune.



FIG. 1.—Girl aged 19, second day of disease.

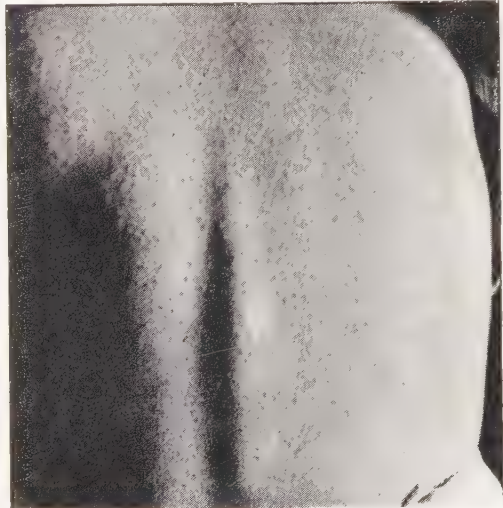


FIG. 2.—Girl aged 6, fourth day of disease.

Dr. D. S. Wilkinson has made the interesting suggestion that this might be a cercarial dermatitis, as described by Cort (1950). The reservoir concerned has been carefully examined and cannot support any snails to act as intermediate hosts to cercariae.

REFERENCES.

- CORT, W. W. (1950) *Amer. J. Hyg.*, **52**, 251.
SCHUPPLI, R. (1947) *Dermatologica*, **94**, 44.

Carcinoma Erysipelatodes.—Dr. N. A. THORNE (for Dr. W. J. O'DONOVAN).

Mr. C. L—, aged 81, states that his general health has been good in spite of operations for removal of adenoma of the prostate and repair of an inguinal hernia nineteen years ago, and the occurrence eight years ago of a gastric ulcer. He gives no history of injury to the scalp, but about twenty years ago he first noticed a small swelling on the right anterior part of the scalp which gradually increased in size, and in its earlier stages was apparently translucent. Fourteen years ago it broke down, discharging blood and "coffee material," and this has happened several times since. Two years ago the swelling was lanced, but has since slowly increased in size. Follow-

ing the shock of his daughter's sudden death eight months ago, he observed a pink discoloration on his forehead which has gradually spread downwards on to his face. He has experienced a burning sensation at times over his face, and stiffness of the eyelids. There has been some loss of weight during the past year.

Family history.—One son has died of a pathological fracture of the leg due to secondary neoplasm, and a daughter has died following an operation for an "ulcer of the rectum."

On examination.—There is a tumour on the right anterior parietal region of the scalp measuring $3.5 \times 3.5 \times 1.6$ cm. It is of irregular outline, firm but slightly fluctuant, not attached to the underlying bone, and covered with normal skin except on its right margin, where there is a superficial ulcer spreading on to the scalp, measuring 1.3×2.6 cm. Over the left vertex and passing backwards towards the occiput there is an S-shaped infiltrated erythematous band on which a few hairs are growing.

Spreading down over the face from the upper forehead as far as the neck, but sparing the distal one-third of the nose, the upper lip and the area below a line drawn from each angle of the mouth to the corresponding angle of the jaw, is an erythematous eruption with a definite circinate and slightly raised margin. There is infiltration of the affected skin, especially of the eyelids, which are prevented from opening fully. Eyelashes are still present. Over the affected region are several areas of normal skin, the largest being above the left eyebrow. Telangiectases are also visible.

The lymph glands of both posterior triangles are enlarged, some having already become matted together. No lymphadenopathy can be detected elsewhere. Apart from some seborrhoeic warts the rest of the skin is normal. General examination fails to reveal any gross physical signs.

Investigations.—Blood count within normal limits. Blood urea 45 mg. per 100 ml. Blood Wassermann negative. Urine normal. X ray chest normal. Barium meal: slight irregularity of posterior aspect of the lesser curve of the stomach but no ulcer seen.

Histology (Dr. D. J. O'Brien).—(a) Piece of trabeculated polygonal cell carcinoma, probably squamous carcinoma, from flat lesion of scalp. (b) Small group of polygonal carcinoma cells in lymphatics of dermis of portion of skin from face.

Comment.—Küttner (1924) named the condition erysipelas carcinomatosus, a term since discarded as being genetically incorrect. The name carcinoma erysipelatodes was first used by Rasch (1931). In the English literature 6 cases are recorded, 1 each by Parkes Weber (1933), and Vonno (1933), who both favour the term carcinoma telangiectaticum, 2 by Gordon (1932 and 1937), and one each by Goldsmith (1929) and Barber (1932). All were females, and the condition was associated either with a primary carcinoma of the breast or with Paget's disease of the nipple. In all but one case the skin manifestations occurred close to the primary growth—the exception being Goldsmith's case, where blood-borne metastases appeared in the skin of the scalp.

In this patient no primary neoplasm could be found in the common visceral sites, e.g., breast, stomach, lung or colon, so that it would appear that the primary must have developed in the wen or atheroma.

Although Shattock (1897) pointed out that the common wen was a cyst, arising in most cases from a hair follicle and not from a sebaceous gland, a confusion of terms has since existed in the literature. Love and Montgomery (1943), in their paper on epithelial cysts, studied 271 cases seen in the Mayo Clinic during 1939-40. Histological examination in 88 cases showed 51 to be epithelial cysts, of which 2 were of traumatic origin. 4 cases (1.5% of the total), showed malignant changes: 2 of these were basal-cell carcinomata arising from sebaceous cysts and 2 were squamous-cell carcinomata arising from true epithelial cysts. They concluded that trauma and irritation played a minor role in the development of malignant changes.

Caylor (1925) reviewed 236 cases of sebaceous cysts without making the distinction between these and epithelial cysts and stated that 3.4% showed malignant changes

Other American authorities have produced even higher rates of malignancy, but similar figures have not been recorded amongst those cases reviewed in this country.

I think that in the present case an epithelial cyst has undergone malignant changes. Neoplastic cells have then spread by the lymphatics to glands in the neck and to the skin of the greater part of the face; further invasion of the blood capillaries has given rise to telangiectases.

REFERENCES.

- BARBER, H. W. (1932) *Proc. R. Soc. Med.*, **25**, 670.
 CAYLOR, H. D. (1925) *Ann. Surg.*, **82**, 164.
 GOLDSMITH, W. N. (1929) *Brit. J. Derm.*, **41**, 270.
 GORDON, H. W. (1932) *Proc. R. Soc. Med.*, **25**, 1551.
 ——— (1937) *Ibid.*, **30**, 983.
 KÜTTNER, H. (1924) *Beitr. klin. Chir.*, **131**, 7.
 LOVE, W. R., and MONTGOMERY, H. (1943) *Arch. Derm. Syph., Chicago*, **47**, 185.
 RASCH, C. (1931) *Brit. J. Derm.*, **43**, 351.
 SHATTOCK, S. G. (1897) *J. Path. Bact.*, **4**, 412.
 VONNO, N. G. VAN (1933) *Brit. J. Derm.*, **45**, 423.
 WEBER, F. P. (1933) *Ibid.*, **45**, 418.

Parapsoriasis en plaques, with Retiform Lesions. Dr. E. WADDINGTON.

Mrs. H. G—, aged 47. Eighteen years ago noticed a non-irritating scaly patch on the right buttock. Since then similar scaly areas have developed on the buttocks, thighs, trunk and arms. The most recent lesion appeared a year ago on the back of the left thigh. The patches have never disappeared, although temporary improvement followed a course of ultraviolet light.

She first attended hospital eighteen months ago because of increasing irritation on the buttocks, and she had also noticed that these lesions had become brighter in colour during the last few months.

On examination.—There are numerous erythemato-squamous plaques on the trunk and limbs. The face, hands and feet are spared. The majority of the plaques are yellow, and the surface is covered with small adherent scales. They are of varying size and irregular shape, and coalescence of the plaques has produced polycyclic lesions. There is no infiltration. On the upper part of the left thigh there is a retiform lesion, the meshes are erythematous and the skin is atrophic. On the buttocks the lesions are similar. There is telangiectasia and adherent scaling, and the skin is pleated like cigarette paper, although there is no atrophy.

Biopsy (Dr. I. Whimster) *from the right buttock shows:*

Epidermis: Slightly hyperkeratotic and hyperplastic. The basal layer is largely depigmented, and contains many vacuolated cells.

Dermis: Occupying the upper third, there is a band of inflammatory cells and very numerous melanophores, and in this region the connective tissues are degenerate.

Comment.—The majority of the lesions are typical of Brocq's parapsoriasis en plaques, but on the buttocks and upper part of the left thigh they are of the rare retiform variety. These lesions closely resemble poikiloderma atrophicum vasculare, although there are no lichenoid papules characteristic of that condition. The patches on the buttocks and thigh remained unaltered for over sixteen years, and then the patient noticed the colour change, and complained of increasing irritation.

These symptoms may be significant.

Lapière (1948) attempted to distinguish between the parapsoriasis of Brocq and the clinically similar premycotic erythema. He was able to show that there are certain features which favour a diagnosis of premycosis, and among these he mentions the development of a reticulated appearance and the onset of pruritus. Koil (1938*a* and *b*) reviewed the literature, and came to the conclusion that Brocq's parapsoriasis en plaques and the retiform type with its transitions into poikiloderma represent phases of a single condition that terminates in mycosis fungoides.

In view of Lapière's work I think this is a premycosis, and it seems probable that the lesions will first develop into a poikiloderma atrophicans vasculare before their final evolution into mycosis fungoides.

REFERENCES.

- KEIL, H. (1938a) *Arch. Derm. Syph., Chicago*, **37**, 465.
 (1938b) *Ibid.*, **38**, 545.
 LAPIÈRE, M. S. (1948) *Arch. belg. Derm. Syph.*, **4**, 40.

Dr. C. H. WHITTLE: We have a man aged 32 with four years' history of parapsoriasis of this type. There are scaly sheets of erythema on the trunk and thighs, with atrophy and retiform changes. The histopathology gives a picture resembling lichen planus. Treatment with thorium-X painting has resulted in complete resolution of the treated lesions, with no change in the untreated ones.

Molluscum Sebaceum Kerato-acanthoma, Benign Epithelioma. Dr. C. H. WHITTLE and Dr. A. LYELL.

A. W—, a coal merchant, aged 55. (Seen first 6 February 1952.)

The lesion on the left cheek started as a pimple which he thinks followed injury with a razor. In 6 weeks it reached a diameter of 2.3 cm., was circular, raised 0.4 cm., with a rounded, smooth, shiny, skin-coloured edge and granulating crater in centre. There was no significant regional lymph-gland enlargement.

The biopsy (section shown) confirms the diagnosis and shows acanthotic hyperplasia with marked hyperkeratosis amounting in places to horny plugs. The tumour is continuous with the epidermis at several points. The base of the tumour is well defined, and remains confined to the level of the dermis and dermal appendages. There is fairly dense cellular reaction in the dermis, chiefly lymphocytic, but including eosinophiles and polymorphs. The vessels are dilated, and there is some oedema at the subpapillary and papillary levels.

Molluscum Sebaceum Kerato-acanthoma, Benign Epithelioma. Dr. C. H. WHITTLE and Dr. A. LYELL.

J. B—, a stableman, aged 54. (First seen 14 February 1952.)

The spot on the right side of the nose started 24 January 1952 and grew rapidly. It is now a raised, dome-shaped circular skin-coloured lesion 1.5 cm. diameter, with a shiny edge standing 0.4 cm. above the surface and with a central crater 0.6 cm. diameter. A week ago it measured 1.3 cm. diameter. No significant lymph-gland enlargement.

Biopsy (section shown) confirms the diagnosis. It shows an acanthoma with well-differentiated and fairly uniform cell structure with much hyperkeratosis. There is moderate lymphocytic infiltration in the papillary layer and predominantly polymorph infiltration between the tumour cells, amounting almost to micro-abscesses. Mitotic activity is comparatively slight.

Comments.—We show these cases as typical examples of a series of twenty which we have collected since our attention was drawn to the condition by Musso, who showed a case here in 1950, commented on by Rook, by Whimster and by Gordon (1951, *Brit. J. Derm.*, **63**, 151). The condition has been fully described since by Rook and Whimster (1950, *Arch. belges Derm. Syph.*, **6** 3, 137).

The clinical features are remarkably constant: they are rapid growth, an appearance closely resembling squamous carcinoma, and a benign course. The histological features invariably suggest to the pathologist—unless he has been forewarned—the diagnosis of well-differentiated keratinizing squamous carcinoma. This is understandable, because in their actively growing phase these cells will show very numerous and sometimes irregular mitoses. But they are not anaplastic and the growing epithelial cords do not transgress the dermal boundary. Without going into the theory of their nature (e.g., Lever, W. F., 1949, *Histopathology of the Skin*, Lippincott)

London, p. 271) we believe they are benign epitheliomata, i.e., benign tumours of epithelial origin, in the sense used by Jadassohn, and by Brooke in "epithelioma adenoides cysticum," and in contrast with the more invasive squamous carcinoma.

In two at least of our twenty cases the lesions have already disappeared without treatment, unless the trauma of biopsy be regarded as effective treatment. (Biopsy section of one of these two shown herewith.)

We have without doubt in the past irradiated or excised a large number of such lesions which would have regressed without our interference.

I wonder if Dr. Ferguson Smith's cases of multiple self-healing epitheliomata, in spite of their familial tendency, are really very different from these kerato-acanthomata. In their short histories, in the pictures of the lesions and in the histopathology (1934, *Brit. J. Derm.*, 46, 519) they suggest a close resemblance to MacCormac's original description (1936, *ibid.*, 48, 626) and to our cases. Also compare Somerville and Milne's case, 1950, *ibid.*, 62, 485.

Postscript (25.iii.52).—Both lesions have dwindled: the first is now 1.6 cm. diameter and nearly flat.—C. H. W.

Dr. A. LYELL: Dr. J. L. Moffatt and I went through the slide boxes and found 20 cases whose sections and clinical histories conformed with this diagnosis, and we found two quite interesting points. The first was that of the 20 cases only 5 were women, and the other point was that most of them came between the ages of 65 and 70. The exposed parts of the body were the ones chiefly affected, face, neck, hand or back of the fingers, and in three cases two lesions were present at the same time.

Dr. I. B. SNEDDON: Like Dr. Whittle, since my attention was drawn to this condition by Drs. Musso, Rook and Whimster, I have seen a fair number of cases. Dr. Whittle has not mentioned treatment. I have left some 6 or 8 of the cases alone after taking a biopsy, and the lesions disappeared within 3 or 4 months but left an ugly depressed scar, sometimes with a slightly raised border. I think one must do something more than leave them alone. Recently I have been excising the whole area when they are small, but when they are large I curette them and that leaves a better scar.

Dr. MARTIN BEARE: In Belfast we have collected about 65 of these tumours in the past three years. Our attention was originally drawn to this condition by Dr. Dowling. We have found that the incidence is 10% of the number of basal and squamous-celled carcinomata of the skin, so that they are extremely common. We have left two or three of them alone and these have disappeared. They had biopsy, but that was the only form of "treatment." Recently we have treated them by cutting off the top with a scalpel and stopping the bleeding with light cautery, no attempt being made to destroy the whole tumour. The cosmetic result from this slight operation is very good. They have all disappeared. Some 20 or more have been treated by this method.

The PRESIDENT: The results of leaving them alone are not very happy; they do leave a scar. The only reason for withholding treatment has been to bring home the fact that they disappear spontaneously, but it would be nice to have some standard method of treatment which would give a reasonable result. I have treated my cases with a single dose of x rays smaller than that required for a basal-cell epithelioma of equal size. I have been satisfied with the results.

Dr. J. E. M. WIGLEY: I freeze the whole area solid with ethyl chloride and curette it. I have seen one or two in which there has been no scar.

Dr. A. J. ROOK: We have curetted about 20 with a very satisfactory cosmetic result.

Dr. D. S. WILKINSON: I have known one or two disappear very satisfactorily in the early stages after application of carbon dioxide snow.

The PRESIDENT: Now that we may treat them I am sure we are all very relieved. We did not like just leaving them to take care of themselves.

Dr. H. T. CALVERT: They respond to podophyllin.

Dr. BEARE: I tried to reproduce these lesions by making a filtrate of tumour tissue and injecting this into patients and into myself, but nothing happened.

The following cases also were shown:

Keratoderma Blennorrhagica.—Dr. D. S. WILKINSON.

Neurofibromatosis of Recent Development. Dr. R. G. HOWELL (for Dr. G. B. DOWLING).

Pemphigus Foliaceus.—Dr. D. I. WILLIAMS.

Atrophic Scleroderma.—Dr. C. D. CALNAN (for Dr. I. MUENDE).

Case for Diagnosis. ? **Polyarteritis Nodosa.**—Dr. J. G. HOLMES (for Dr. G. B. MITCHELL-HEGGS).

CURRENT LITERATURE

RETICULUM CELL SARCOMA. K. B. LAWRENCE and N. LENSON. (1952) *J. Amer. med. Ass.*, 149, 361.

A girl aged 16 with anaplastic reticulum cell sarcoma involving the supraclavicular glands and inaccessible to surgery received 1000 r of x-ray therapy. There was no evidence of recurrence 13 years later. Reviewing the literature the authors point out that the survival rate of lymphosarcoma is usually inversely proportional to the dose of x ray employed. In a reported series of 136 cases the recurrence rate after 2 years was 20% when 2000 to 3000 r had been given, but 72% after 1000 r. The age of the patient also influences the prognosis, and in another series of cases no patient under 30 had survived 10 years. Malignant lymphomas are encountered in a strictly localized form in about 10% of cases. Surgical extirpation is then the treatment of choice.

A. J. R.

LOCAL EFFECT OF COMPOUND F ON REACTIONS TO MOSQUITO BITES. L. GOLDMAN. (1952) *J. Amer. med. Ass.*, 149, 265.

Compound F injected intradermally inhibits both the immediate and late reactions to mosquitoes biting over the area in which the injection was made. This local inhibitory effect persists for at least 4 months.

A. J. R.

PERIPHERAL NEURITIS IN SYSTEMIC LUPUS ERYTHEMATOSUS. R. H. HELTFESTALL and G. S. C. SOWRY. (1952) *Brit. med. J.*, 1, 525.

Systemic lupus erythematosus is described in a woman aged 34 in whom the presenting picture was peripheral neuritis. It is considered that the peripheral neuritis was due to ischaemia following vascular lesions in the vessels supplying the nerves.

B. A. T.

FAMILIAL ERYTHEMA NODOSUM. JOHN FRY. (1952) *Brit. med. J.*, 1, 529.

The aetiology of erythema nodosum is discussed. It is a non-specific reaction to a variety of allergens, the most important being the association of erythema nodosum with a primary tuberculous infection. Its relation to acute rheumatism, streptococcal infections, sarcoidosis, sulphonamide hypersensitivity, coccidioidomycosis and a miscellaneous group of conditions is also dealt with. A report is given of three cases occurring simultaneously in one family, tuberculosis being implicated here.

B. A. T.

SEVERE AND FATAL PHENOBARBITONE ERUPTIONS. I. B. SNEDDON and A. W. D. LEISHMAN. (1952) *Brit. med. J.*, 2, 1276.

They describe four cases of severe allergic reactions to phenobarbitone given in therapeutic doses and suggest that the potential dangers of phenobarbitone skin eruptions may not be sufficiently appreciated. *Post mortem* examinations in these cases reveal no specific pathological changes. In one case intravenous A.C.T.H. had a lifesaving effect, but in another cortisone failed.

B. A. T.

CEMENT DERMATITIS. L. P. DE CARVALHO and E. B. NEGREIROS. (1952) *O Hospital*, 41, 495.

The authors investigated 30 cases of vesicular epidermo-dermatitis in cement workers. When patch-tested with 0.5% potassium dichromate solution 29 reacted positively, to cement 25 were positive and 3 reacted to 10% lime. Of 19 patients who later resumed their occupation, 17 rapidly became extremely intolerant. Age and duration of exposure in the occupation did not seem to have any relation to the onset of the condition.

G. W. B.

ORAL B.C.G. IN THE TREATMENT OF LUPUS ERYTHEMATOSUS. L. BAPTISTA and N. BELLIBONI. (1952) *O Hospital*, 41, 503.

A woman aged 52 with classical lesions on the face, present for 2 years, did not respond to injections of sodium salicylate and vitamin C, so was given 0.2 g. B.C.G. orally once a week. There was some improvement after 3 doses, after 6 doses the lesions had practically healed, and

had nearly disappeared completely after the ninth dose. The Mantoux 1/1000 test was positive both before and after treatment. The authors have also found this method of treatment useful in Bazin's disease. G. W. B.

LYMPHADENOSIS CUTIS BENIGNA. L. DE SA PENELLA. (1952) *Actas dermo-sif., Madrid*, 43, 393.

A woman aged 53 whose lesions had appeared 5 years previously had violaceous nodules on the cheeks and chin, some of which appeared to be involuting. In the dermis there were sharply defined nodules consisting mostly of lymphocytes and lymphoblasts enclosing germinal centres. The lesions did not respond to any form of treatment. There is a good general review of the condition. G. W. B.

HISTOPLASMOSIS. G. SCOTTI. (1952) *Dermatologia*, 3, 22.

A good general review of the subject from all aspects.

D. S. W.

A CASE OF ICHTHYOSIS TREATED WITH VITAMIN F99. G. GIARDINO. (1952) *Dermatologia*, 3, 12.

A review of the value of unsaturated fatty acids in the treatment of various conditions, and the best method of giving it, particularly to infants. The author believes that these substances are therapeutically useful in their own right, as well as perhaps having a protective action on vitamins A and E. That these fatty acids, particularly linoleic and linolenic, are essential for the proper metabolism of the body one would not dispute; that they are not absorbed or are diverted in certain diseases it is feasible to suggest; that they are valuable therapeutically is altogether less certain; that, in combination with vitamin A or not, they can be given with success in cases of ichthyosis seems much less likely; but from his own results the author thinks they are worth trying. D. S. W.

LEMON DERMATITIS. V. PUGLISI. (1951) *G. ital. Derm. Sif.*, 92, 237.

A very full and careful account of the subject dealing with the lemon itself and the biochemistry of its constituents, and the industrial processes concerned with its cultivation, marketing and by-products. Dermatitis seen in lemon workers can be grouped as specific and non-specific. Cases of the latter arise from contact with fertilizers, insecticides, fungi, alkaline solutions, and by trauma from knives or splinters of wood. The dermatitis of specific cause may arise from citric acid and the essential oils (terpenes) acting as irritants; or allergic reactions to citric acid, α -limonene, or both of these may occur together. These generally show themselves as vesicular or bullous eruptions, sometimes as nodules. Even the consumers are not entirely free from hazard, since they may acquire allergic reactions to constituents of the lemon by contact or ingestion. Most common are a nodular eruption, cheilitis or a pigmenting dermatitis. A rather frightening list of yet further troubles which may arise from eating lemons is given. Although not likely to be common in this country, it is as well to recognize the possibility of their existence and the forms that allergic reactions to lemons may take. There is an extremely detailed account of the constituents and biochemistry of each part of the fruit, which is of considerable interest. D. S. W.

VARIATIONS IN THE PLASMA PROTEINS IN ACUTE PYOGENIC ECZEMATIDES. V. PUCINELLI. (1951) *G. ital. Derm. Sif.*, 92, 285.

Correlation of the change in the euglobulin fractions and other liver function tests in 8 patients with pyogenic eczematides. The α -globulin levels were on the whole raised in the acute stage of the attack, and the γ -globulins in the stage of repair and resolution. There was no obvious correlation between the other tests, but further investigations are needed on the same lines.

D. S. W.

IN VITRO ACTIVITY OF SOME ANTIBIOTICS ON ERYSIPELOTHRIX RHUSIOPATHIAE. P. MORONI. (1951) *Dermatologia*, 2, 263.

Continuing his investigations described in an earlier paper, the author finds that of tyrothricin, terramycin, bacitracin and furazine, tyrothricin and terramycin appear the most useful; both, however, are less effective than penicillin. Tyrothricin can only be applied locally. The author's experiments were conducted *in vitro*, and he refrains from pronouncing on their therapeutic action clinically. D. S. W.

PSORIASIS: GEOGRAPHICAL AND ETHNOGRAPHICAL CONSIDERATIONS, AETIOLOGY AND INTERNAL TREATMENT. A. MARCHIONINI and H. W. FEIER. (1951) *Dermatologia*, **2**, 299.

Psoriasis is commoner among white races than others, wherever they are living. A sunny climate may help to cure but does not prevent recurrences or the onset of the disease. Geographical considerations may be deceptive; local customs of clothing, bathing, etc., may act as subsidiary influences. The authors believe psoriasis to be a cutaneous reaction to a number of causal factors in the presence of a "soil" constitutionally disposed in a manner not yet defined. It seems likely that this condition is carried as an irregular hereditary dominant genotype. The authors discuss the various groups of influences which may cause the disease to appear, and various forms of internal treatment which have been in vogue, ranging from arsenic to the vitamins and the steroids. They adopt a very conservative attitude to the value of these respective agents, pointing out that they are all usually more effective the more generalized the psoriasis. It seems fair to add that extensive psoriasis is, in any case, more likely to improve than to deteriorate under any form of treatment, as long as this is harmless.

D. S. W.

A CASE OF ACANTHOSIS NIGRICANS. V. RESTA. (1951) *Arch. ital. Derm. Syph.*, **24**, 275.

A description of a case of acanthosis nigricans with photographs leave little doubt of the diagnosis. This condition, in a girl of 17, was associated with pulmonary tuberculosis. The author discusses theories of origin of this disease and points out the rarity of association with tuberculosis. It is not easy to be sure that this was not fortuitous, but three such cases of the association have been reported. The patient was treated with streptomycin, and the author quotes a case of hypertrichosis in a child of 27 months with tuberculous meningitis treated with streptomycin and a further case of hirsuties in a woman following this antibiotic. These cases, unfortunately, throw no light upon the cause of acanthosis nigricans and similar melanoses, but merely extend the field of speculation. The author inclines to the theory of an endocrine factor with or without a naevoid background.

D. S. W.

HYPERGLYCAEMIA IN NICOTINAMIDE TREATMENT OF PATIENTS WITH SKIN TUBERCULOSIS. U. SILVESTRI and P. GRIFA. (1951) *Arch. ital. Derm. Syph.*, **24**, 260.

Following earlier investigations into the action of nicotinamide in the treatment of tuberculosis of the skin, the authors studied the action of this substance on blood-sugar levels. After intravenous injection of 3 to 6 g., they found that a rise in the blood sugar took place, usually towards the end of the first hour after injection. The nicotinamide also appeared to increase the height of the blood-sugar curve following both glucose and adrenaline. This hyperglycaemia was transitory. The authors do not, in this article, pursue the reason for its therapeutic action.

D. S. W.

EFFECTS OF ACTH AND CORTISONE ON CERTAIN DISEASES AND PHYSIOLOGIC FUNCTIONS OF THE SKIN. I: EFFECTS OF ACTH. M. B. SULZBERGER, G. C. SAUER, F. HERRMANN R. L. BAZER and I. L. MILBERG. (1951) *J. invest. Derm.*, **16**, 323.

This is the record of first attempts with a new drug. As far as the clinical part is concerned it would have added to the interest if we could have been told whether the cases are related in chronological order. For traces of the familiar but inexplicable "brilliant cure—improved—better than nothing—no effect—made worse" sequence can be made out in the groups that contain more than one case.

The physiological findings, expressed very tentatively, are that ACTH accelerates peripheral circulation, shortens wheal absorption time, increases sweating and electronegativity in the terminal portion of sweat ducts, and diminishes sebaceous secretion. No immunological changes nor influence on eczematoid reactivity.

J. H. T. D.

PAIN-THRESHOLD MEASUREMENTS ON HUMAN SKIN FOLLOWING THE APPLICATION OF TOPICAL ANALGESICS. J. D. HARDY, C. B. POTELUNAS and M. D. MEIXNER. (1951) *J. invest. Derm.*, **16**, 369.

Neither method nor apparatus are described in sufficient detail to justify the reviewer asking his readers to pay any attention to this paper. For the conclusions—that the lip, but not the skin, can be anaesthetized by ointment; and that freezing with ethyl chloride produces anaesthesia by virtue of its chilling effect on the sensory nerves—are hardly of sufficient interest by themselves.

J. H. T. D.

PITUITARY-ADRENOCORTICAL FUNCTIONING IN PATIENTS WITH ATOPIC DERMATITIS.T. H. STERNBERG, P. BUTLER and M. C. ZIMMERMANN. (1951) *J. invest. Derm.*, **16**, 355.

The eosinophil count is considered to be the most reliable index of pituitary-adrenocortical activity. The cases of flexural prurigo studied here gave the same response as the controls to adrenalin injected, but an opposite reaction to exposure to a very hot humid atmosphere—that is to say, the eosinophil count rose after an hour in a room at 110° F. and 90% humidity.

Since the response to adrenalin was normal it is considered that the adrenal cortex and anterior pituitary are probably functioning correctly and that the disorder must lie in the medulla or hypothalamus. Without the hypothalamus the "alarm reaction" cannot take place and, since it is not sufficient to prevent it by severing and sealing off the pituitary stalk, it is suggested that the hypothalamus may possibly have an internal secretion. Perhaps this is exhausted in atopics, or possibly it is the adrenal medulla that wearies of fruitless demand.

It happened that one of the patients taking part in this investigation was subsequently treated with ACTH. His skin remains perfectly clear on a maintenance dose of 40 mg. daily. This circumstance is thought to support the hypothesis of a relationship between the adrenocortical system and "atopy."

J. H. T. D.

**CYST FORMATION, ACNEIFORM LESIONS AND HAIR GROWTH FOLLOWING INTRA-
DERMAL INJECTION OF STAPHYLOCOCCI IN SENSITIZED RABBITS.**J. G. HOPKINS, J. T. WELD and W. M. HUBER. (1951) *J. invest. Derm.*, **16**, 339.

This study began as an attempt to reproduce the findings of Boe (1946), who described certain immunological phenomena associated with the intradermal injection of *Staphylococcus aureus* into the skin of rabbits sensitized to it and, at the same time, to make a histological study of the lesions.

100 million cocci, live or dead, are injected intradermally. On the first occasion only a transient red spot results. If the injections are repeated at 10-day intervals the reaction becomes progressively more severe, finally producing a substantial infiltrated nodule which resolves very slowly. The nodule is seen to contain pus, and sometimes has a few horny plugs in the dilated follicles on its surface. At one stage, not very closely determined, the lesion becomes surrounded with a ring of rapidly growing hairs.

Section showed that in nearly all cases neighbouring follicles were found to be contributing to the structure of the cyst which came eventually to surround the debris and to transport it to the surface.

A primary injection of 1000 million staphylococci might produce a small abscess but not one with an epithelial cyst wall, though in two cases of a second injection the cyst wall did develop. *B. coli* did not provoke a cyst wall, nor did turpentine or other foreign bodies.

The work certainly revives interest in the influence of bacteria in acne; but anyone repeating the experiment would doubtless add the sex hormone factor to his protocol.

J. H. T. D.

A NEW METHOD TO INCREASE THE PERMEABILITY OF HARD KERATIN STRUCTURES.S. ROTHMAN and C. L. TASCHDJIAN. (1951) *J. invest. Derm.*, **17**, 9.

Lithium bromide in concentrated aqueous solution at 110° F. will shrink woollens and release the so-called "permanent set" of hair. The authors therefore visualized an "opening up" of the molecular structure of keratin, and speculated on the possibility that fungicides might penetrate better. Results so far obtained are promising. It seems that it is possible to wet an infected nail with a combined solution of lithium bromide and fungicide and then to paint over it with clear nail varnish.

J. H. T. D.

**ADAPTATION OF THE ADAMSTONE-TAYLOR FROZEN SECTION TECHNIQUE FOR RAPID
DIAGNOSIS OF SKIN LESIONS.**

H. MESCON, H. BEERMAN and F. D. WEIDMAN. (1951)

J. invest. Derm., **16**, 429.

The tissue is cut without any preparation and is kept frozen until immersion in the fixative. But it is not made clear why the section does not stick to the knife or to the little refrigerated shovel on which it is transported around the laboratory. Nor is it explained exactly why sections of 5-7 μ are possible with this method in contrast with the 15-20 μ normal for an ordinary freezing microtome.

If it is true that satisfactory permanent H. & E. preparations can be available within 10 minutes of the biopsy it is obvious that, except in the hands of the very few technicians who can cut 3-5 μ sections, the paraffin embedding technique is obsolete.

J. H. T. D.

CHROME ULCERS OF THE SKIN AND NASAL SEPTUM AND THEIR RELATION TO PATCH TESTING. W. F. EDMUNDSON. (1951) *J. invest. Derm.*, 17, 17.

"If . . . a break in the continuity of the skin . . . is contaminated by a chrome salt . . . ulceration develops. This ulceration is cone-shaped, has a hard thick edge, tends to burrow downward instead of laterally, takes the shape of the original opening in the skin surface and heals very slowly."

285 men were examined. We are not told what proportion this number bore to the total affected or the total exposed to the hazard. Naturally one wants to ask whether everybody with a scratch who is exposed to chrome develops an ulcer.

Some had ulceration of the nasal mucosa, some of the skin, and some of both. The numbers in each category are given, but no means of telling how many had, for example, mucous membrane lesions only. The table showing anatomical distribution also leaves many interesting points obscure for the same kind of reason.

Of 33 white workers 2 gave positive patch tests: in 24 "non-white" workers patch tests were all negative. These numbers are probably enough to confirm that chrome ulceration is not necessarily associated with epidermal sensitization. J. H. T. D.

CHEMOTHERAPY OF ECZEMA-DERMATITIS. (1) ORAL ADMINISTRATION OF SULFAPYRIDINE: ANALYSIS OF 301 CASES. L. J. A. LOEWENTHAL. (1951) *J. invest. Derm.*, 16, 387.

The success of sulphapyridine in the treatment of dermatitis herpetiformis is unquestioned: it has also been claimed by reliable observers in a variety of cases of chronic eczema.

The scope of this investigation included (1) metastatic eczema in contact dermatitis ("generalized sensitization") and in exacerbations of chronic lichenified eczema ("autosensitization eczema"), (2) infectious eczematoid dermatitis (defined by the author as "an eczematous reaction in an area contaminated with infectious (*sic*) discharges, e.g., around persistent axillary boils (*sic*) or the pinna in a case of chronic discharging otitis media"), (3) infantile eczema, (4) flexural prurigo whether consecutive to infantile eczema or not, (5) nummular eczema, and (6) eczema occurring in pregnancy. The author's conception of acute (47 cases) and chronic (98 cases) endogenous eczema is not very clearly expressed, and the reviewer is surprised to note the number of patients (40) "who developed a local eczema from the application of acriflavine to minor injuries of the skin." Bichromate is also mentioned in this connection, but not nickel.

All the same, in his classification of his clinical material, whether we agree with it or not, the author has given us a valuable and enlightening glimpse of his own thoughtful point of view.

The results are expressed in terms of "improvement," which is here taken to mean "an appreciable degree of symptomatic relief along with objective improvement, in chronic cases significant only when it exceeds that of spontaneous remissions."

Unfortunately it is not at all clear to the reviewer whether the author means that 57% improved during the first week, 25% continued to improve in the second and so on; or if in 57% of the cases improvement was already evident in the first week, in 25% not till after 2 weeks of treatment. This may well be important, though it doesn't seem to the reviewer that any pharmacological significance at all can possibly be attached to improvement during the week following a consultation with a clinician having the personal qualities that can be inferred from the literary style of this paper. J. H. T. D.

SOME INVESTIGATIVE STUDIES OF PIGMENTED NAEVI WITH CUTANEOUS MICROSCOPY

L. GOLDMAN. (1951) *J. invest. Derm.*, 16, 407.

These close-up views of moles are no more attractive to the eye than the author's argument is to the intellect. J. H. T. D.

EXAMINATION OF THE EPIDERMIS BY THE STRIP METHOD OF REMOVING HORN LAYERS. I: OBSERVATIONS ON THICKNESS OF HORN LAYER AND ON MITOTIC ACTIVITY AFTER STRIPPING. H. PINKUS. (1951) *J. invest. Derm.*, 16, 383.

When transparent adhesive tape is stuck on the skin and peeled off it brings with it an incomplete single layer of stratum corneum. Repeat the process approximately 20 times and you reach the stratum granulosum—which resists any further decortication. Following this operation the deeper layers of the rete set to work to repair the damage, and at the end of 48 hours mitoses are seen in one in every 66 nuclei. This compares with figures attributed to Thuringer of 1:2414 for normal adult scalp and 1:268275 (surely a misprint but of course commendably precise) for the ear. J. H. T. D.